DOI: 10.7860/JCDR/2022/57814.16818

Original Article

Others Section

Assessment of Reliability of Advanced Lipid Parameters for Premature Coronary Artery Disease in Young Indians: A Case-control Study

RAHUL PATIL[1], SHEETAL KUDINEERAKATTE[2], VIKRANT VIJAN[3], DIMPU EDWIN[4]

ABSTRACT

Introduction: Coronary Artery Disease (CAD) appears even in patients with normal level of conventional lipid parameters. But due to lack of specific guidelines on Indian population, involving detection of advanced lipid indices, has resulted in inadequate finding, management, and control of cardiovascular disease risks. This emphasises the need of advanced lipid indices for prediction of CAD at younger age.

Aim: To evaluate the reliability of advanced lipid indices compared to conventional lipid parameters for diagnosis of CAD. Also, to determine the effectiveness of advanced lipid indices in screening young Indian for the risk of Premature CAD (PCAD).

Materials and Methods: A case-control study was conducted at a tertiary care centre in Bengaluru, Karnataka, India, between January 2020 to January 2022. The study enrolled total 983 subjects which were divided into cases and controls. The estimation of usual lipid profile {Triglycerides (TG), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), and Total Cholesterol (TC)} and advanced lipid parameters, oxidised LDL, Apolipoprotein A1 (Apo A1), lipoprotein (a), small density LDL (Sd-LDL), and Apolipoprotein B-100 (Apo B) was studied for each enrolled individual. These lipid parameters were used to calculate various lipid indices like Lipid Pentad Index (LPI), Lipid Tetrad Index (LTI), Atherosclerotic Index (AI), and Advanced Atherosclerotic Index (AAI); and TC/HDL ratio. Statistical analysis was performed using Chi-square test, Fisher's-exact test, multivariate logistic regression, and Student's t-test/ Analysis of Variance (ANOVA) test.

Results: Mean age of participants in case group was 32.31±5.42 years and in control group was 32.13±5.21 years. Among case group, 427 (88.04%) enrolled males had PCAD. In case group, total 45 (9.28%) had diabetes, 51 (10.51%) had family history of PCAD and 230 (47.42%) patients were smokers. The values of TC (p-value=0.009), LDL (p-value <0.001), Apo A1 (p-value <0.001), HDL (p-value<0.001) were significantly lower among cases compared to controls, lipoprotein (a) (p-value=0.04), Sd-LDL (p-value <0.001), TG (p-value <0.001) were significantly higher among cases compared to controls. Among the calculated lipid indices, the values of AI (p-value <0.001), LTI (p-value <0.001), LPI (p-value=0.001) and AAI (p-value=0.01) were significantly higher among cases as compared to controls.

Conclusion: Advanced lipid indices are statistically more reliable than conventional lipid parameters. Newer advanced lipid indices are effective in screening young Indian individuals for the risk of PCAD.

Keywords: Atherosclerosis, Cardiovascular disease, Indian population, Lipid indices, Young patients

INRODUCTION

Coronary Artery Disease (CAD) has become a leading cause of morbidity and mortality all over the world and in developing countries like India. At present, India has become cardiovascular disease capital of the world. Indians are 3-4 times at higher risk of CAD than Americans, six times higher than Chinese, and 20 times higher than Japanese population. Even young Indians (≤45 years) are prone as a community for CAD [1,2]. PCAD is defined as cardiac events occurring before the age of 55 years in men and 65 years in women, but severe PCAD is considered as the occurrence of Ischaemic Heart Disease (IHD) at much younger age that is 40 years [3]. Studies reported that CAD is affecting Indians 5-10 years earlier than western population where the incidence of PCAD is upto 5% as compared to 12-16% in Indians. In Indian, the average age of first heart attack is 10 years earlier compared to western population, and of that 25% are occurring before the age of 40 years [4,5].

As previous landmark studies on prevention and treatment of CAD have mostly engaged Caucasian population. Therefore, western guidelines derived from these studies have failed in both primary and secondary prevention of cardiovascular disease in Indian population [1,6]. The reason for this failure might be the clear and fundamental differences in the pathophysiology and clinical features of the cardiovascular disease in Asian Indian [7]. Hence, there is a need to consider cardiovascular disease among Asian Indians as distinct entity in comparison to Caucasians. On 1st April 2017, a first-of-its-kind registry was started at our centre, exclusively for PCAD patients (males <40 years, females <45 years), under the title of project PCAD to study the incidence, prevalence, clinical profile, and uniqueness of PCAD among Indians. During the enrolment for that registry, a significant observation was made that CAD occurs even in patients with normal level of conventional lipid parameters such as LDL and HDL, and the same has been reported in many previous studies [6]. Similarly, a study by Bansal SK et al., suggested advanced lipid parameters {i.e. oxidised low density lipoprotein (Ox-LDL), lipoprotein (a), Apoprotein-A1 (Apo-A1), small dense LDL (Sd-LDL), Apoprotein-B (Apo-B)} as better predictors and markers for amplifying high degree of prematurity, morbidity and mortality of CAD in Indian population, as compared to conventional lipid parameters [8].

Furthermore, the manifestation of CAD in normolipidaemic individuals provide the insight to the researchers to look beyond the conventional lipid parameters. Therefore, several lipid indices such as AI, LTI, LPI, and AAI, which are derived from the conventional/advanced lipid parameters, are developed to determine the association of lipid risk factor and CAD [9,10]. Moreover, due to non availability of Indian population specific guidelines, including detection of advanced lipid

parameters, has resulted in incomplete detection, treatment, and control of cardiovascular disease risks. Therefore, the present study was designed to prove the reliability of advanced lipid parameters compared to conventional lipid parameters for atherosclerosis and CAD. This study was also aimed to determine the effectiveness of advanced lipid indices in screening young Indian for the risk of PCAD.

MATERIALS AND METHODS

This case-control study was conducted at a tertiary care cardiac centre in Bengaluru, Karnataka, India, between January 2020 to January 2022. The study was approved by the Medical Ethics Committee of the Institute (MEC11B-Thesis/P24,2020) and the written informed consent was obtained from all participants before enrolment.

Inclusion criteria: Patients aged ≤40 years of either gender and who were diagnosed with IHD, with documented indication of acute coronary syndrome (unstable angina, ST elevation/non ST elevation myocardial infarction) or chronic stable angina with clinical evidence of CAD were included as cases. Age matched individuals from the general population who were defined as CAD free, based on clinical history or detailed examination were included as controls in the present study.

Exclusion criteria: Patients with a history of chronic alcoholism, concomitant liver, or kidney disease and acute or chronic infection; patients taking hypolipidaemic drugs, oral contraceptives, or hormone replacement therapy and patients unwilling to give informed consent were excluded from the study.

Sample size: Sample size of 1000 (500 in each group) was estimated in the present study, based on the results of a previous study which showed a difference of 7 mg/dL on Apo A1, with 90% statistical power and 5% level of significance [11].The study included a total of 983 subjects, which were divided into two groups:

1. Case group (n=485)- Patients who were diagnosed with PCAD (acute coronary syndrome and/or chronic stable angina) were included as cases.
2. Control group (n=498)- Age matched individuals from the general population who were defined as CAD free based on clinical history or detailed examination.

All enrolled patients were asked to complete a proforma covering demographic data such as age, gender, medical history, smoking habits, and medical treatment. A standardised diagnostic protocol was followed consisting of physical examination and laboratory testing in a fasting state for all the study subjects.

The fasting blood sample (5 mL) was taken from antecubital vein for the estimation of conventional lipid profile (TG, HDL, LDL, TC) and advanced lipid profile (Ox-LDL, Apo A1, lipoprotein (a), Sd-LDL, and Apo B-100). Normal range for all the parameters in given in [Table/Fig-1].

Parameter	Name of the test	Normal range
Triglycerides	Enzyme-linked immunoassay method	<150 mg/dL
High density cholesterol		40 to 60 mg/dL
Low density cholesterol		70 to 130 mg/dL
Total cholesterol		<200 mg/dL
Very-low-density lipoprotein		2 to 30 mg/dL
Non-high-density cholesterol		<130 mg/dL
Apolipoprotein A1		Males: 75-160 mg/dL Females: 80-175 mg/dL
Lipoprotein (a)		<30 mg/dL
Apolipoprotein B-100		<130 mg/dL
Oxidised low-density cholesterol		<60 U/L

[Table/Fig-1]: Lipid parameters along with their reference values measured in present study.

Sd- LDL was indirectly calculated using the following formula [12]:

Sd-LDL=0.94Chol–0.94HDL–0.19TG/Apo B–0.09Chol+0.09HDL–0.08TG

These lipid parameters were used to calculate various lipid indices like LPI, LTI, AI, AAI; and total cholesterol/HDL ratio.

Formulas for calculation of various lipid indices are as follow: [12].

1. **AI**=(Log [TG/HDL])
2. **LTI**=TC×TG×lipoprotein (a)÷HDL
3. **LPI**=TC×TG×lipoprotein (a)×Apo B÷Apo A1
4. **AAI**={Ox LDL×lipoprotein (a)×Apo B}÷(Apo A1×Sd LDL)

STATISTICAL ANALYSIS

Statistical software R-version 4.1.3 (R Core Team, 2022, Vienna, Austria) was used for statistical analysis. All categorical data were compared between case and control by frequency and percentage with Chi-square test. The continuous parameters such as age, lipid profile, and advanced lipid indices were compared by mean±SD with Student's t-test. The predictability of advanced lipid indices was compared by Receiver Operating Characteristic (ROC) curve analysis. Sensitivity, specificity, and Area Under the Curve (AUC) were reported with 95% confidence interval. Univariate odd ratio of PCAD for 10 unit increase of AAI, sex, age and diabetes were estimated by contingency table analysis. Further an adjusted logic regression was performed to assess the confounding effects of age, sex, diabetes on the association of PCAD and AAI. A p-value <0.05 was considered as statistical significance.

RESULTS

A total of 983 subjects were enrolled for the study and were divided into case group (comprised of 485 patients) and control group (comprised of 498 individuals).

Mean age of the study population was 32.22±5.31 years (32.31±5.42 years for case group and 32.13±5.21 years for control group). Among case group, 427 (88.04%) enrolled males had PCAD and only 58 (11.96%) females reported PCAD. In case group, total 45 (9.28%) had diabetes, 51 (10.51%) had family history of PCAD and 230 (47.42%) patients were smokers. However, in control group, only 4 (0.8%) individuals had diabetes, 64 (12.85%) were smokers and none reported family history of PCAD [Table/Fig-2].

Variables	Case (N=485)	Control (N=498)	p-value
Age, years (mean±SD)	32.31±5.42	32.13±5.21	0.320[£]
Age distribution years, n (%)			
≤25	58 (11.96%)	57 (11.45%)	0.454[¥]
26-30	113 (23.30%)	125 (25.10%)	
31-35	188 (38.76%)	177 (35.54%)	
36-40	126 (25.98%)	139 (27.91%)	
Gender distribution, n (%)			
Male	427 (88.04%)	369 (74.1%)	<0.001[¥]
Female	58 (11.96%)	129 (25.9%)	
Risk factors, n (%)			
Diabetes	45 (9.28%)	4 (0.8%)	<0.001[¥]
Smokers	230 (47.42%)	64 (12.85%)	<0.001[¥]
Family history of PCAD	51 (10.51%)	0	<0.001[¥]
Hypertension	54 (11.13%)	9 (1.8%)	<0.001[¥]

[Table/Fig-2]: Baseline demographic characteristics.
PCAD: Premature coronary artery disease; [¥]Chi-square test, [£]Student t-test, level of significant p-value <0.05

Mean TC level of cases was 141.07±45.11 mg/dL, whereas that of control was 145.72±36.78 mg/dL (p-value=0.009). Mean LDL cholesterol of cases was 84.66±39.25 mg/dL while that of control was 93.04±31.57 mg/dL (p-value <0.001). Though statistically significant but the values of TC (p-value=0.009) and LDL

(p-value <0.001) were significantly lower among cases compared to controls. However, HDL (p-value <0.001) were significantly lower among cases compared to control and triglycerides (p-value <0.001) were significantly higher among cases compared to controls. The ratio of total cholesterol/HDL was significantly higher among cases compared to controls (p-value <0.001) [Table/Fig-3].

Variables	Overall (N=983)	Case (N=485)	Control (N=498)	p-value (t-test)
Total cholesterol, mg/dL	143.42±41.15	141.07±45.11	145.72±36.78	0.009
High density lipoprotein, mg/dL	29.17±10.42	27.26±12.19	31.03±7.91	<0.001
Low density lipoprotein, mg/dL	88.91±35.79	84.66±39.25	93.04±31.57	<0.001
Triglycerides, mg/dL	160.97±104.37	177.04±116.61	145.31±88.22	<0.001
Non high density lipoprotein, mg/dL	115.14±41.22	114.39±42.91	115.86±39.53	0.577
Very low-density lipoprotein, mg/dL	38.51±195.18	35.54±23.61	41.4±273.33	0.634
Total cholesterol/ High density lipoprotein ratio	5.31±2.23	5.73±2.61	4.92±1.69	<0.001

[Table/Fig-3]: Comparison of conventional lipid indices (Mean±SD) among case and control group.
Independent t-test, level of significant p-value <0.05

Among the lipid indices, the values of AI (p-value <0.001) higher in control, LTI (p-value <0.001), LPI (p-value=0.01) and AAI (p-value=0.01) were significantly higher among cases compared to controls. Lipoprotein (a) (p-value=0.04) was significantly higher among cases compared to controls [Table/Fig-4].

Variables	Overall (N=983)	Case (N=485)	Control (N=498)	p-value (t-test)
Apolipoprotein A1, mg/dL	93.43±22.83	88.3±21.92	98.42±22.61	<0.001
Apolipoprotein B, mg/dL	92.22±29.12	93.58±30.45	90.89±27.73	0.148
Lipoprotein (a), mg/dL	42.98±50.71	46.34±53.39	39.7±47.78	0.04
Small density Low Density Lipoprotein, mg/dL (sd-LDL)	35.2±22.1	40.53±24.89	30.01±17.53	<0.001
Oxidised Low Density Lipoprotein, mg/dL (Ox-LDL)	58.98±81.53	64.15±101.46	53.96±55.31	0.052
Atherosclerotic Index (AI)	0.7±0.67	0.7772±0.28	0.6214±0.28	<0.001
Lipid Tetrad Index (LTI)	40217.31±74003	50371±88484	30328±54750	<0.001
Lipid Pentad Index (LPI)	13.48516± 2864159	1664378± 3421134	1040900± 2149081	0.001
Advanced Atherosclerotic Index (AAI)	71.96±101.91	80.62±109.5	60.44±89.75	0.01

[Table/Fig-4]: Comparison of advanced lipid indices (Mean±SD) among case and control group.
Independent t-test, level of significant p-value <0.05

Indices like AI, AAI, LTI, LPI were compared as diagnostic marker for PCAD. AI was found to be most powerful diagnostic marker among all above, exhibited 70% sensitivity but only 54% specificity [Table/Fig-5].

Estimated odds ratio (OR) by univariate logistic regression of AAI for gender (OR:1.04, CI:0.66 -1.63), diabetes (OR:7.16, CI:2.51-20.4), and smoking (OR:6.98, CI:4.52-10.79) showed higher risk for PCAD. For every 10 units increase in AAI, there was 2% increase in probability of acquiring PCAD. However, when these three factors were adjusted, the adjusted impact of AAI on PCAD was not changed. Hence, these three factors are not confounding between AAI and PCAD.

Parameters	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	AUC (95% confidence interval)
Atherosclerotic Index (AI)	0.7 (0.66-0.74)	0.54 (0.49-0.58)	0.66 (0.62-0.69)
Lipid Tetrad Index (LTI)	0.61 (0.57-0.66)	0.59 (0.54-0.63)	0.63 (0.59-0.66)
Lipid Pentad Index (LPI)	0.61 (0.57-0.65)	0.59 (0.55-0.63)	0.62 (0.59-0.66)
Advanced Atherosclerotic Index (AAI)	0.56 (0.51-0.60)	0.48 (0.44-0.53)	0.50 (0.47-0.54)

[Table/Fig-5]: Specificity and sensitivity of advanced Lipid indices for prediction of PCAD in young Indian.
ROC curve was used for prediction

DISCUSSION

Despite conventional lipid profile (TC, LDL, HDL, and TG) being an established tool for early prediction and management of cardiovascular disease. A significant number of cardiovascular events remain unaddressed in Indian populations [13]. Lipids are carried within lipoprotein which carry lipid particles that vary in size, density, charge, core lipid composition, specific apolipoproteins, and function [10]. Despite availability of the large pool of information on lipids and its estimation, it is still unclear that how to utilise advanced lipid analysis for primary and secondary prevention of cardiovascular disease. Moreover, new biomarkers require standardisation and comparability, accessibility, clear indications, and lastly demonstrating cost-effectiveness [14,15].

Literature state that advanced lipids have the potential to improve risk prediction and management of cardiovascular disease [6,16]. However, current prevention guidelines are not supporting these, owing to lack of grade-A level of evidence. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in 2013 did not issue any recommendation for Apo B, LDL, or lipoprotein (a) due to lack of randomised trials evidence for these measures as well as non HDL as goals of therapy [3]. Therefore, advanced lipids are promising biomarkers, but they are not currently recommended as routine tools for CVD risk assessment and management.

In present study, the patient population was predominantly males in case and control groups (88% vs 74.1%). Similarly, there was disproportionate number of smokers and diabetic patient population. However, statistical analysis proved that these three factors are not confounding between AAI and PCAD. They are risk factors but not confounders. In a pilot study by Bansal SK et al., they studied a small sample of 120 patients among whom maximum patients were in the age of 36-45 years (80 out of 120, 66.67%), whereas the age cut-off (40 year) and average age was much lower in present study (31.22 years) hence present study population was more representative of younger population. In the study by Bansal SK et al., the values of TC (p-value <0.001), TG (p-value=0.032), LDL (p-value <0.001), OX LDL (p-value <0.001), Lipoprotein (a) (p-value <0.0001), and Apo B (p-value <0.001) were significantly higher while HDL (p-value<0.01), SD LDL (p-value <0.001), and Apo A1 (p-value <0.001) were significantly lower in the cases as compared to the controls [12].

However, contrary to the traditional belief of high TC and LDL cholesterol being most important lipid markers both for primary and secondary prevention of CAD, present study showed that values of TC (p-value=0.009) and LDL cholesterol were significantly lower among cases compared to controls (p-value <0.001). The Lipid ratios of TC/HDL was significantly higher among cases compared to controls (p-value <0.001). Among the lipid indices the values of AI (p-value <0.001), LTI (p-value <0.001), LPI (p-value=0.001) and

AAI (p-value=0.001) were significantly higher among cases compared to controls.

In the study by Bansal SK et al., the values of AI, LTI, LPI, and AAI were significantly higher in cases as compared to controls. Out of all the indices newly defined AAI showed maximum correlation (p-value <0.001, r=0.737) with the disease as compared to AI (p-value <0.001, r=0.520), LTI (p-value <0.001, r=0.677) and LPI (p-value <0.001, r=0.622) [12].

In present study, advanced lipid parameters such as Sd-LDL (p-value <0.001), lipoprotein (a) (p-value=0.04), were significantly higher among cases compared to control. However, no statistically significant difference was noted for Ox-LDL (p-value=0.052) and Apo-B (p-value=0.148) among cases and controls. In contrast to present study findings, Bansal SK et al., reported statistically significant difference (p-value <0.0001 for all) among cases and controls for all advanced lipid parameters suggesting more predictability of these parameters for PCAD [8].

Furthermore, the values of lipid indices such as AI, LPI, LTI and AAI which were calculated from various lipid parameters were significantly higher in PCAD patients in Indian population as compared to the controls (p-value <0.001). From the results of the present study, it emerges that advanced lipid parameters such as AI, LPI, LTI, and AAI has better discriminating value in CAD patients as compared to conventional indices.

In addition, as parameters involved in calculation of these indices are genetically determined, it may more precisely illuminate higher incidence, severity, and prematurity of CAD. They may be proved as an important screening test for early detection and intervention in CAD patients in the Indian population. However, their importance as markers of dyslipidaemia in premature CAD patients have to be further explored in larger and heterogenous patients and should be validated before clinical implementation.

Limitation(s)

Sample size in present study was less than the calculated sample size. Also, there was significant difference in sex ratio among cases and controls. However, statistical analysis proved that gender was not confounding between AAI and PCAD i.e. they are predictors but not confounders.

CONCLUSION(S)

Advanced lipid parameters like Apo A1, Apo B, lipoprotein (a), Sd-LDL, and Ox-LDL were statistically more reliable than conventional lipid parameters such as HDL, LDL, TC, and TG. Newer lipid incorporating advanced lipid indices such AI, LPI, LTI, and AAI are effective in screening young Indian individuals for risk of PCAD. Present study was single centre study predominantly involving urban and semi-urban population. Hence, a multicentric study across different parts of the country would help to generalise these findings specifically for Indian population. Therefore, future studies should assess and validate the potential of advanced lipids in assessment and prevention of cardiovascular disease and its management.

REFERENCES

[1] Kumar AS, Sinha N. Cardiovascular disease in India: A 360 degree overview. Med J Armed Forces India. 2020;76(1):1.
[2] Bhat KG, Kandanuru KH, Kumar A, Swamy AJ, Kumar MN, Sharma P, et al. Coronary artery disease in young Indians: A different entity. Int J Med Res Prof. 2019;5(5):01-10.
[3] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;62(16):e147-e239.
[4] Negus BH, Willard JE, Glamann DB, Landau C, Snyder II RW, Hillis LD, et al. Coronary anatomy and prognosis of young, asymptomatic survivors of myocardial infarction. Am J Med. 1994;96(4):354-58.
[5] Enas EA, Kannan S. How to beat the heart disease epidemic among South Asians: Advanced Heart Lipid Clinic; 2005.
[6] Sharma M, Ganguly NK. Premature coronary artery disease in Indians and its associated risk factors. Vascular Health and Risk Management. 2005;1(3):217.
[7] Dawber TR, Kannel WB, Revotskie N, Stokes III J, Kagan A, Gordon T, et al. Some factors associated with the development of coronary heart disease—six years' follow-up experience in the Framingham study. American Journal of Public Health and the Nations Health. 1959;49(10):1349-56.
[8] Bansal SK, Agarwal S, Daga MK. Conventional and advanced lipid parameters in premature coronary artery disease patients in India. J Clin Diag Res. 2015;9(11):BC07.
[9] Dobiásová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate inapob-lipoprotein-depleted plasma (FERHDL). Clinical Biochemistry. 2001;34(7):583-88.
[10] Morais CAdS, Oliveira SHV, Lima LM. Lipid Tetrad Index (LTI) and Lipid Pentad Index (LPI) in healthy subjects. Arquivos Brasileiros de Cardiologia. 2013;100:322-27.
[11] Suresh K, Chandrashekara S. Sample size estimation and power analysis for clinical research studies. J Hum Repro Sci. 2012;5(1):07.
[12] Bansal SK, Agarwal S, Daga MK. Advanced atherogenic index for the assessment of consolidated lipid risk in premature coronary artery disease patients in India. J Lab Physicians. 2016;8(02):077-84.
[13] Harada P, Akinkuolie A, Mora S. Advanced lipoprotein testing: Strengths and limitations. Am Coll Cardiol. 2014.
[14] Mudd JO, Borlaug BA, Johnston PV, Kral BG, Rouf R, Blumenthal RS, et al. Beyond low-density lipoprotein cholesterol: Defining the role of low-density lipoprotein heterogeneity in coronary artery disease. J Am Coll Cardiol. 2007;50(18):1735-41.
[15] Genest J, McPherson R, Frohlich J, Anderson T, Campbell N, Carpentier A, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult–2009 recommendations. Canadian J Cardiol. 2009;25(10):567-79.
[16] Nelson RH. Hyperlipidemia as a risk factor for cardiovascular disease. Primary Care: Clinics in Office Practice. 2013;40(1):195-211.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
2. Associate Professor, Department of Biochemistry, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
3. Cardiologist, Department of Cardiology, Vijan Heart Centre, Nashik, Maharashtra, India.
4. Assistant Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rahul Patil,
Associate Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India.
E-mail: dr.rahulspatil85@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 23, 2022
- Manual Googling: Jul 29, 2022
- iThenticate Software: Aug 29, 2022 (25%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 17, 2022**
Date of Peer Review: **Jun 02, 2022**
Date of Acceptance: **Aug 07, 2022**
Date of Publishing: **Sep 01, 2022**