

# Carotid Artery Ultrasonography as a Screening Tool for Predicting Coronary Artery Disease: A Cross-sectional Study from Hilly State of Northern India

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## ABSTRACT

**Introduction:** Coronary Artery Disease (CAD) is a major cause of morbidity and mortality worldwide; therefore, early diagnosis plays a crucial role in managing patients with CAD. Multidetector Computed Tomography (MDCT) allows non invasive visualisation of coronary arteries but has limited availability, involves radiation, and is costly. Carotid artery atherosclerosis can be assessed by Ultrasound (USG) in terms of Carotid Intima-media Thickness (CIMT) and carotid plaque assessment. These carotid USG parameters are associated with CAD and can be used to predict CAD in high-risk patients.

**Aim:** To study the association and correlation between carotid artery atherosclerosis USG parameters (CIMT and carotid plaque) and CAD, using Computed Tomography Coronary Angiography (CTCA) as a reference.

**Materials and Methods:** A cross-sectional study was conducted from January 2020 to October 2021 in the Department of Radiodiagnosis at Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. In the present study, 31 patients with suspected CAD were enrolled. All patients underwent CTCA followed by carotid artery USG within two weeks. The association and correlation between carotid artery atherosclerosis on USG and CAD on CTCA were examined. Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and accuracy were calculated using CTCA as the reference

standard. Categorical data were analysed using the Chi-square test, with a p-value of <0.05 considered statistically significant.

**Results:** The mean age of the patients was 54.06±10.79 years. The CAD was observed in 14 (45.1%) cases, of which 13 (92.8%) had significant CAD. Nine patients had raised CIMT, of which eight had CAD. Raised CIMT and CAD showed a significant association with sensitivity, specificity, PPV, NPV, and accuracy of 57.14%, 94.12%, 88.89%, 72.73%, and 77.42%, respectively. A positive correlation was found between CIMT values and the number of vessels with significant CAD ( $r=+0.67$ ). A total of 7 patients (22.5%) had the presence of carotid plaque, of which 6 (88.57%) had significant CAD. A significant association was found between CAD and the presence of carotid plaque. Carotid plaque had sensitivity, specificity, PPV, NPV, and accuracy of 50%, 100%, 100%, 70.83%, and 77.42%, respectively, in predicting CAD. A positive correlation was observed between carotid plaque burden and the number of vessels with significant CAD ( $r=+0.56$ ).

**Conclusion:** There is a significant association between carotid ultrasonography parameters (i.e., CIMT, carotid plaque) and CAD. CIMT is a more sensitive parameter than carotid plaque in predicting CAD. However, carotid plaque is more specific for predicting CAD. Carotid artery ultrasonography can be used as a screening tool for predicting CAD and should be included in the work-up of patients with suspected CAD.

**Keywords:** Carotid intimal-media thickness, Carotid plaque, Computed tomography coronary angiography, Coronary artery disease

## INTRODUCTION

Coronary Artery Disease (CAD) is a major cause of morbidity and mortality worldwide. Therefore, early diagnosis plays a crucial role in managing patients with CAD. Conventional Invasive Coronary Angiography (ICA) is the gold standard for diagnosing known or suspected CAD. MDCT is an alternative imaging modality that allows non invasive visualisation of coronary arteries [1]. Recent studies using 64-slice MDCT coronary angiography have shown sensitivity up to 94% and specificity up to 97% for detecting significant coronary stenosis [2]. The atherosclerotic process occurs simultaneously in the carotid, cerebral, and coronary arteries [3]. Carotid artery atherosclerosis can be assessed in terms of CIMT and carotid plaque evaluation. Several studies have shown an association between carotid artery atherosclerosis on USG and CAD on coronary CTCA [4-6]. These studies concluded that increased carotid IMT and plaques are associated with the presence and severity of CAD on CT Angiography [4-6]. Furthermore, carotid artery USG can be used for CAD screening in asymptomatic patients with multiple coronary risk

factors [6]. Assessing coronary atherosclerosis with MDCT coronary angiography provides detailed information; however, it involves radiation and higher costs. In contrast, ultrasonographic assessment offers the advantage of being truly non invasive, inexpensive, mobile, radiation-free, and a powerful tool in assessing atherosclerosis [7]. Therefore, CIMT and carotid plaque, due to their association with CAD, can be particularly useful as an initial step in selecting high-risk patients requiring further cardiovascular evaluation. Since the present study had not been conducted in our state as per the literature to date, it was undertaken to compare carotid USG findings with CT for detecting CAD. Thus, the present study will promote USG screening of carotid arteries in patients with suspected CAD in locations where angiography is not available, leading to timely referrals, early detection, and management of CAD, thereby reducing mortality and morbidity.

## MATERIALS AND METHODS

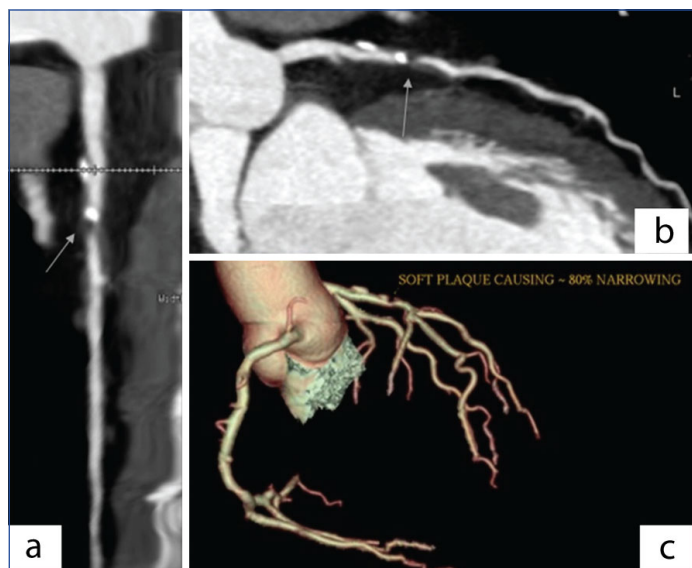
After obtaining informed consent, a cross-sectional study comprising 31 patients was conducted over a 22-month period from January

2020 to October 2021 in the Department of Radiodiagnosis, Indira Gandhi Medical College, Shimla, a tertiary institute in a hilly state of North India. The study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Institutional Ethics Committee.

**Inclusion and Exclusion criteria:** The inclusion criteria for the study included patients with angina on exertion with a positive stress or Treadmill Test (TMT) for inducible angina, patients with angina and equivocal TMT, and asymptomatic patients with a positive stress test. Patients with absolute contraindications to CTCA, such as allergy to contrast, hyperthyroidism, abnormal renal function tests (serum creatinine >1.5 mg/dL), previous coronary artery bypass graft or coronary stents, inability to hold breath for 10-15 seconds, cardiac arrhythmias, elevated heart rate, contraindications to beta blockers, already diagnosed cases of CAD on treatment and multiple myeloma, and pregnant females were excluded from the study.

**Study Procedure**

**MDCT coronary angiography:** The patients underwent coronary angiography using a 64-slice MDCT scanner (Lightspeed VCT-XTe, GE Medical Systems). MDCT angiograms were assessed on a 3D workstation (Advantage Windows version 4.5, CardIQExpress 4.0, GE Healthcare). Coronary arteries were analysed for the degree of stenosis and the number of vessels involved [Table/Fig-1a-c]. Stenosis was quantified as per [Table/Fig-2]. Patients were classified as positive for significant or obstructive CAD if there was ≥ 50% stenosis in any coronary artery. Patients were categorised as having single, two, or three-vessel disease based on involvement of the Right Coronary Artery (RCA), Left Anterior Descending Artery (LAD), Left Circumflex Artery (LCX), and the Left Main Artery (LMA). Lesions detected in any branch of these vessels were also considered under main vessel involvement. Following CTCA, carotid artery USG was performed on all patients.



**[Table/Fig-1]:** A 41-year-old male who presented with stable angina and had positive TMT test. Straight a); curved multiplanar reconstruction b); Volume rendered images c); of LAD revealed partially calcified plaque (arrow) in LAD causing 70-90% luminal narrowing.

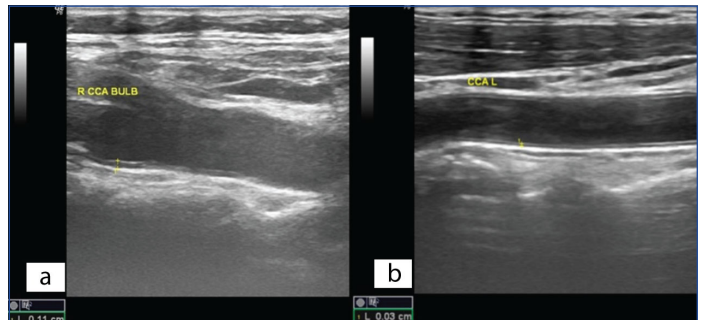
Percentage luminal narrowing	Quantification of stenosis
No narrowing	No stenosis/CAD
<50%	Non significant mild stenosis or non obstructive CAD
50-70%	Obstructive CAD with moderate stenosis
>70%-99%	Obstructive CAD with severe or critical stenosis
Complete occlusion	

**[Table/Fig-2]:** Quantification of stenosis.

**Carotid artery ultrasonography:** Carotid artery ultrasonography was conducted using the GE Logic P6 machine. Patients were positioned in a supine posture with their heads slightly hyperextended and their necks rotated in the direction opposite to the probe. Carotid artery USG was performed on both sides using a linear array transducer with a fundamental frequency of 10-13 MHz. The following parameters were documented:

**Common Carotid Artery (CCA)- Intima-media Thickness (IMT) Measurement:**

For CIMT assessment, the distance between the blood-intima and media-adventitia interface of the far wall of the common carotid artery was measured at three plaque-free sites [Table/Fig-3a,b]. The scanning encompassed both carotid arteries. The average CIMT was calculated by determining the mean of these three values in the bilateral carotid arteries. An intima-media thickness of less than 1 mm was considered normal [8].



**[Table/Fig-3]:** A 62-year-old female who presented with complaint of chest pain on exertion and had CAD. Carotid ultrasonography image (a) revealed raised right CIMT (0.11 cm). Left CIMT was normal (0.03 cm) (b).

**Carotid plaque screening:** Carotid plaque is defined as the presence of focal wall thickening that is at least 50% greater than that of the surrounding vessel wall, or as a focal region with CIMT greater than 1.5 mm that protrudes into the lumen and is distinct from the adjacent boundary. During the plaque screening, the bulb and internal carotid arterial segments were carefully examined. The carotid plaque volume was determined by scanning to identify the largest plaque extension in transverse views of each plaque in the common and internal carotid arteries bilaterally. The anteroposterior and transverse diameters were multiplied to obtain the area in mm [3]. The same plaque was scanned to find the largest extension in the longitudinal view; the craniocaudal length thus obtained was multiplied by the plaque area to determine the plaque volume in mm [8]. The total plaque burden was assessed by summing the total plaque volume in both carotid arteries.

**STATISTICAL ANALYSIS**

The data were analysed using Statistical Package for Social Sciences (SPSS) software (IBM Corp, 2013; Version 22.0; Armonk, NY). The data were entered into a Microsoft excel spreadsheet and presented in the form of percentages, sensitivity, specificity, PPV, NPV, and accuracy. Categorical data were analysed using the Fischer’s-exact test, where an appropriate p-value of <0.05 was considered statistically significant.

**RESULTS**

In the present study, the mean age of the patients was 54.06 ± 10.79 years. Most patients, 17 (54%), were in the age group of 51-60 years. Of the 31 study subjects, 21/31 (67.7%) were males, and 10/31 (32.3%) were females [Table/Fig-4].

Age group	Frequency (n)	Percentage (%)
<40 years	1	3.2
41-50 years	9	29.0
51-60 years	17	54.8
>60 years	4	12.9

**[Table/Fig-4]:** Age distribution of study subjects (N=31).

The CAD was found in 14 (45.1%) cases out of the 31 cases, and 13 (92.8%) had significant CAD on MDCT ( $\geq 50\%$  stenosis in any coronary artery). The mean age of patients with significant CAD was 59 years. Out of the 14 patients with CAD, eight had a history of smoking, showing a significant association between CAD and smoking (p-value 0.03). A total of 5 (55.55%) patients with raised CIMT were hypertensive in the study. A significant association was found between raised CIMT and hypertension with a p-value  $<0.012$ .

Among these 13 cases, three-vessel disease was present in 3 (23.07%) cases, two-vessel disease in 3 (23.07%) cases, and one-vessel disease in 7 (53.84%) cases. Among the major coronary vessels, LAD was involved in all cases with CAD seen in 14 (45.2%), with 70-99% luminal narrowing in 13 (92.8%) cases.

Nine patients had raised CIMT, out of which eight patients had CAD. There was a stronger association of CAD with CIMT than with carotid plaque (p-value=0.009  $> 0.02$ ) [Table/Fig-5].

Variables	CAD				p-value		
	Significant CAD			Insignificant CAD		No CAD	
CIMT (N=31)	Raised	3 (1 VD)	1 (2 VD)	3 (3 VD)	1	1	*0.009
	Normal	6			0	16	
Carotid plaque (N=31)	Present	6			1	0	*0.02
	Absent	7			0	17	
Luminal narrowing (N=31)	Nil	7			0	17	0.03
	<25%	3			1	0	
	25-50%	3			0	0	
Plaque character (N=31)	Soft	5			0	0	0.2
	Soft and calcified	1			1	0	

[Table/Fig-5]: Association between significant CAD and various USG parameters. VD: Vessel disease; \*Fisher's-exact test

The mean CIMT was higher in CAD patients at 0.92 mm compared to patients without CAD, which was 0.28 mm (p-value  $< 0.004$ ).

A significant association between CAD and raised CIMT was observed [Table/Fig-6]. A positive correlation was found between CIMT values and the number of vessels with significant CAD as shown in [Table/Fig-7] ( $r=+0.67$ ). CIMT exhibited sensitivity, specificity, PPV, NPV, and accuracy of 57.14%, 94.12%, 88.89%, 72.73%, and 77.42%, respectively, in diagnosing CAD [Table/Fig-8].

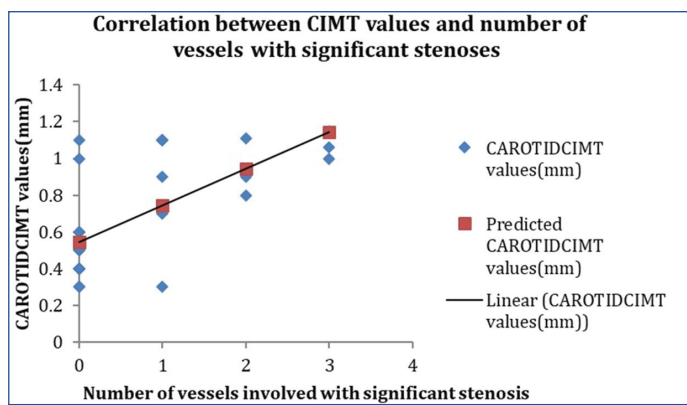
Variables	CAD		p-value	
	Present	Absent		
	n (%)	n (%)		
CIMT (N=31)	Raised	8 (57.1%)	1 (5.9%)	*0.004 S
	Normal	6 (42.9%)	16 (94.1%)	
Carotid plaque (N=31)	Present	7 (50%)	0	*0.001 S
	Absent	7 (50%)	17 (100%)	

[Table/Fig-6]: Cross tabulation between CAD and various carotid USG parameters.

\*Fisher's-exact test; CIMT: Carotid intimal-media thickness; CAD: Coronary artery disease

The presence of carotid plaque showed sensitivity, specificity, PPV, NPV, and accuracy of 50%, 100%, 100%, 70.83%, and 77.42%, respectively, in diagnosing CAD [Table/Fig-8]. A positive correlation was observed between carotid plaque burden and the number of vessels with significant CAD as shown in [Table/Fig-9] ( $r=+0.56$ ).

The presence of raised CIMT had a stronger association with CAD than the presence of carotid plaque. The sensitivity and NPV of raised CIMT were higher than those of carotid plaque. However, the specificity and PPV of carotid plaque were higher. In all cases with carotid plaque, there was some degree of luminal narrowing. Thus, luminal narrowing exhibited the same diagnostic performance as



[Table/Fig-7]: Correlation between CIMT and number of vessels with significant CAD. A positive correlation was found between CIMT and significant CAD with a correlation coefficient ( $r = +0.67$ ).

carotid plaque. A significant association could not be established between the nature of carotid plaque and the presence of CAD (p-value=0.2, [Table/Fig-5]).

### DISCUSSION

The CTCA is the preferred imaging modality for non invasive visualisation of coronary arteries. As the atherosclerotic process occurs simultaneously in the carotid and coronary arteries [3], many studies have shown an association between carotid artery atherosclerotic parameters and CAD on CTCA [9-12]. Early carotid artery atherosclerosis is typically measured in terms of CIMT and carotid plaque. CIMT is a valid marker of early atherosclerosis and has the potential to detect cardiovascular disease. It has been proven to be a useful non invasive means of quantitatively assessing the amount of atherosclerosis in the carotid arteries [9,10]. The advantage of B-mode USG lies in its ability to image atherosclerosis within the arterial wall rather than in the lumen of the artery. Carotid plaque predominantly represents intimal thickening with foam cells, smooth muscle cells, macrophages, lipid core, and fibrous cap, depending on the stage of plaque development. Several recent studies have also shown a significant relationship between carotid plaque and the presence of occlusive CAD [11,12].

The CAD was found in 14 (45.1%) cases, out of which 13 (92.8%) cases had significant CAD. The mean age of patients with significant CAD was 59 years (n=13), which was higher than that of patients with insignificant/no CAD, who had a mean age of 49.7 years (n=18). This finding is consistent with the study conducted by Morito N et al., who observed that the mean age was higher in patients with significant CAD [13].

A total of 5 (55.55%) patients with raised CIMT were hypertensive in the present study. A significant association was found between raised CIMT and hypertension with a p-value  $<0.012$ . The present study aligns with the study conducted by Jeevarethinam A et al., where CIMT was elevated in patients with CAD and hypertension with a p-value  $< 0.01$  [14].

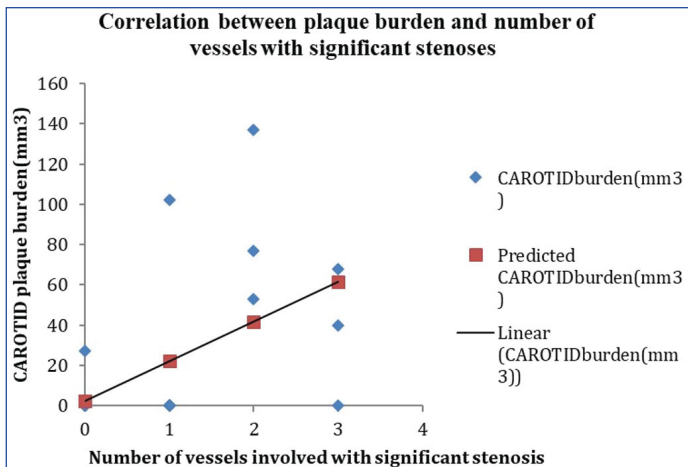
Raised CIMT was found in nine patients, out of which 8 (89%) had CAD. The mean CIMT was higher in CAD patients at 0.92 mm compared to patients without CAD at 0.28 mm (p-value  $<0.004$ ). Jeevarethinam A et al., observed similar results in 150 patients with no history of CAD and found that the mean CIMT was higher in patients with CAD than those without CAD (0.76 vs 0.66 mm) [14].

There was a significant association between raised CIMT and CAD (p-value  $<0.004$ ), and a linear correlation was found between CIMT values and the number of vessels with significant stenosis, with a correlation coefficient (r) of +0.67. In the study conducted by Balbarini A et al., a positive linear correlation between CIMT and CAD was found with a correlation coefficient of +0.43 and p-value  $<0.001$  [15]. Similar results were observed in the present study. Balbarini A et al., also observed that the sensitivity, specificity, PPV, and NPV of CIMT in diagnosing CAD



Variables	True positive	False positive	False negative	True negative	Sensitivity (%) 95% CI	Specificity (%) 95% CI	PPV (%) 95% CI	NPV (%) 95% CI	Accuracy (%) 95% CI
CIMT	8	1	6	16	57.14 (28.86-82.34)	94.12 (71.31-99.85)	88.89 (53.11-98.26)	72.73 (59.01-83.16)	77.42 (58.9-90.41)
Carotid plaque	7	0	7	17	50 (23.04-76.96)	100 (80.49-100)	100	70.83 (58.99-80.39)	77.42 (58.90-90.41)

[Table/Fig-8]: Sensitivity, Specificity, PPV, NPV and accuracy values of different variables.



[Table/Fig-9]: Correlation between carotid plaque and number of vessels with significant CAD. A positive correlation was found between carotid plaque and significant CAD with correlation coefficient ( $r = + 0.56$ ).

were 70.7%, 59.0%, 80.6%, and 45.6%, respectively [15]. The present study had some differences. In their study, any wall lesion  $< 2.5$  mm was considered as increased CIMT, and plaques were defined as any wall lesion with a thickness greater than 2.5 mm. This difference may have led to a higher sensitivity of CIMT in diagnosing CAD in their study compared to ours (57.14%). A similar study was conducted by Cohen GI et al., who studied a total of 150 subjects who underwent both CTCA and carotid USG on the same day. In their study, the PPV and NPV of CIMT  $> 1.5$  mm for CAD were 70% and 67%, respectively [4]. Our study had modest agreement with this.

A total of 7 (22.5%) patients had the presence of carotid plaque, 6 (85.71%) patients with carotid plaque had significant CAD. A significant association was observed between the presence of carotid plaque and the number of vessels with CAD, with a correlation coefficient of  $r=0.56$  and  $p$ -value of 0.001. Similar results were found in the meta-analysis conducted by Bytçi I et al., who established that the degree of atherosclerosis in the carotid arteries and major coronary arteries were correlated ( $r=0.53$ ;  $p=0.001$ ) [16]. In the present study, carotid plaque had a sensitivity of 50%, specificity of 100%, PPV of 100%, and NPV of 70.83%. In a study conducted by Hensley B et al., carotid plaque had a sensitivity of 66.7% and specificity of 92.8% in diagnosing CAD [17]. The present study differed slightly from this study. The lower sensitivity (50%) of carotid plaque in the present study could be attributed to the small sample size. However, the higher specificity (100%) in the present case could be because authors considered even mild narrowing of the vessel as CAD.

Cohen GI et al., studied a total of 150 subjects and found a highly significant relationship between the presence of carotid plaque and CAD with a  $p$ -value of  $< 0.0001$ . In their study, the PPV and NPV of carotid plaque for CAD were 69% and 77%, respectively [4]. The present study also showed slight variance from this study, possibly due to the smaller sample size and CAD being defined as the presence of any degree of narrowing within the coronary vessels. The diagnostic accuracy of carotid plaque in diagnosing CAD was 74.19% in the present study, which was consistent with the study conducted by Morito N et al., who evaluated 116 patients with carotid USG and coronary angiography and predicted an accuracy of 73.9% [13].

Although the present study was conducted with a small sample size, it was able to identify a statistically significant correlation between carotid artery USG and CAD. Therefore, a study with a larger sample size is recommended for validation. For screening a large population without previously known cardiovascular disease, USG can be used as the first-line modality. This approach will lead to timely referrals to higher institutes for treatment, thereby reducing complications and mortality. It will not only improve personal well-being but also reduce the economic burden at the individual and community levels.

### Limitation(s)

The main limitation of the study was the small sample size. Due to the Coronavirus Disease-2019 (COVID-19) pandemic, a smaller number of patients visited the hospital, except for COVID-19-related symptoms or other emergencies. The findings of CTCA were not confirmed with Catheter Angiography, which is the gold standard for confirming vascular stenosis. The results of the study are limited by the nature of the population, as it catered only to symptomatic patients from the local area, and the study did not compare cases with healthy/asymptomatic patients.

### CONCLUSION(S)

The CTCA is a valuable tool for detecting the presence and severity of CAD. However, CTCA is typically performed only when symptoms have already manifested. Given the significant association between carotid artery USG parameters and CAD on CTCA, carotid artery USG can be utilised as a first-line imaging modality for screening asymptomatic subjects, during pregnancy, and at healthcare facilities where CT is not available.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]

- Plagiarism X-checker: Oct 19, 2023
- Manual Googling: Jan 16, 2024
- iThenticate Software: Feb 01, 2024 (13%)

**ETYMOLOGY:** Author Origin**EMENDATIONS:** 6**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. Yes

Date of Submission: **Oct 18, 2023**Date of Peer Review: **Dec 26, 2023**Date of Acceptance: **Feb 02, 2024**Date of Publishing: **Apr 01, 2024**