

Correlation Between Earlobe Crease and Coronary Artery Disease in Indian Population- A Multicentre Experience

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ABSTRACT

Background: Earlobe crease (ELC) has been found to be associated with the presence of coronary artery disease (CAD) in many studies; however, studies from India are limited. The aim of this study was to determine the prevalence of CAD in those with ELC and to assess the correlation of ELC with severity of CAD. **Materials and Methods:** This was a cross-sectional, multicenter study; 1400 patients undergoing coronary angiogram were approached, but 1070 patients were analyzed after excluding patients with ear piercings and other ear diseases. Patients were classified into no ELC, mild ELC, and severe ELC according to Ishi *et al.* **Results:** Seven hundred and eighty patients had CAD proven by coronary angiography. Of these, 74% (580/780) had an ELC either mild or severe. The patients with ELC had a significantly higher incidence of hypertension, diabetes mellitus, and hypercholesterolemia. However, the prevalence of smoking and family history of premature cardiovascular death were similar in both the groups. The prevalence of CAD was found to be significantly higher (odds ratio [OR]: 4.22 [95% confidence interval (CI): 3.18–5.61], $P < 0.0001$) among the patients with ELC (580/698) in comparison to patients without ELC (200/372). The prevalence of multivessel disease (MVD) was found to be significantly higher among the ELC-positive patients than ELC-negative patients (OR: 5.03 [95% CI: 3.61–6.90], $P < 0.0001$). Moreover, MVD was significantly more prevalent in patients (OR: 6.27 [95% CI: 4.23–9.29], $P < 0.0001$) in the severe ELC group (150/190) in comparison to the mild ELC group (190/508). **Conclusion:** ELC is an important clinical sign which should be examined carefully for its presence as well as severity. Both presence and severity of crease were related to occurrence and severity of CAD, respectively, in our study. Long-term cohort studies involving multiple ethnicity populations are necessary to determine the role of ELC in development as well as prognosis of CAD.

KEYWORDS: Coronary angiography, coronary artery disease, earlobe crease, Indian population

INTRODUCTION

Coronary artery disease (CAD) contributes to one of the largest disease burdens in India affecting nearly 1%–2% of the rural population and 2%–4% of the urban population and leading to nearly 26% of the total deaths in India.^[1] The recent ESC guideline on chronic coronary syndrome emphasizes the role of pretest probability in evaluation of CAD. There has been a constant search for some signs which could increase this pretest probability. One such sign is the presence of earlobe crease (ELC).^[2] Anatomically, both the earlobe and heart are supplied by the “end arteries.” Microvascular disease has been found to be behind the development of ELC as has

been found in the development of CAD.^[3] The association between the presence of earlobe crease (ELC) and CAD was first reported by Frank in 1973;^[3] however, the correlation of ELC to CAD has been debated. Studies carried out by Evrengül *et al.*, Edston, Shmilovich *et al.*, Cumberland *et al.*, Mirić *et al.*, Wang *et al.*, Hou *et al.*, Kamal *et al.*, Wu X *et al.*,

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Suen *et al.*, *et al.*,^[4-13] strongly showed that ELC was strongly associated the presence of CAD, while on the other hand, studies carried out by Jorde *et al.*^[14] and Davis *et al.*^[15] negated this hypothesis. The most important drawback of the previous studies was the lack of confirmation CAD by coronary angiogram (CAG), and there have been studies published from India, but they are handful in numbers such as those by Verma *et al.*, Raman *et al.*, and Amit; these studies also established the association of ELC with CAD.^[16-18] The aim of the present study was to find the prevalence of ELC in those with CAD and to establish the relationship between ELC and CAD.

MATERIALS AND METHODS

It was a cross-sectional multicenter observational study, conducted in three tertiary care hospitals of India between June 2016 and August 2018. The three participating centers were LPS Institute of Cardiology, GSVM Medical college, Kanpur. Grant Medical College (GMC), Mumbai, and All India Institute of Medical Sciences (AIIMS), Rishikesh. With confidence interval of 95%, power of 80%, and least extreme odds ratio (OR) of 2, the sample size was kept to 1052.

Inclusion and exclusion criteria

One thousand and four hundred consecutive patients were approached who were admitted to the cardiology facility for coronary angiography for appropriate indications as per the appropriate use criteria of the American Heart Association.^[19] Three hundred and thirty patients were excluded due to ear piercings, diseases or surgery of the external ear, and refusal to give consent. Rest 1070 patients were enrolled in the study following informed consent. The study protocol was approved by the local ethics committee and is summarized in Figure 1.

Earlobe crease

Each of the patients was examined by one independent physician from each center (HK from LPSC, VM from GMC, and DK from AIIMS), and any discrepancy was resolved by sharing images in WhatsApp. As detailed in Figure 1, the absence of crease was awarded zero point; if the crease was present but did not touch both the borders of the earlobe, one point was awarded; if the crease touched both the borders of the earlobe, two points were awarded. Total points including both the earlobes were calculated, and patients have been classified into no ELC (total score: 0), mild ELC (total score: 1–2), and severe ELC (total score: 3–4) according to Ishii *et al.*^[20] Figure 2 illustrates the examples of each classification.

Baseline parameters and risk factors

Demographic characteristics and hematological and biochemical parameters were recorded for all the patients ($n = 1070$). Hypertension (HTN) was defined as blood pressure (BP) more than 130/80 mmHg according to the American College of Cardiology/American Heart Association (ACC/AHA) 2017 guideline.^[21] Diabetes mellitus (DM) was defined as a fasting blood sugar (FBS) >126 mg/dl, postprandial blood sugar >200 mg/dl, or glycosylated hemoglobin >6.5% as per the American Diabetes Association 2019 guideline.^[22] Dyslipidemia was defined as a fasting total cholesterol level of >200 mg/dl according to the consensus statement of the

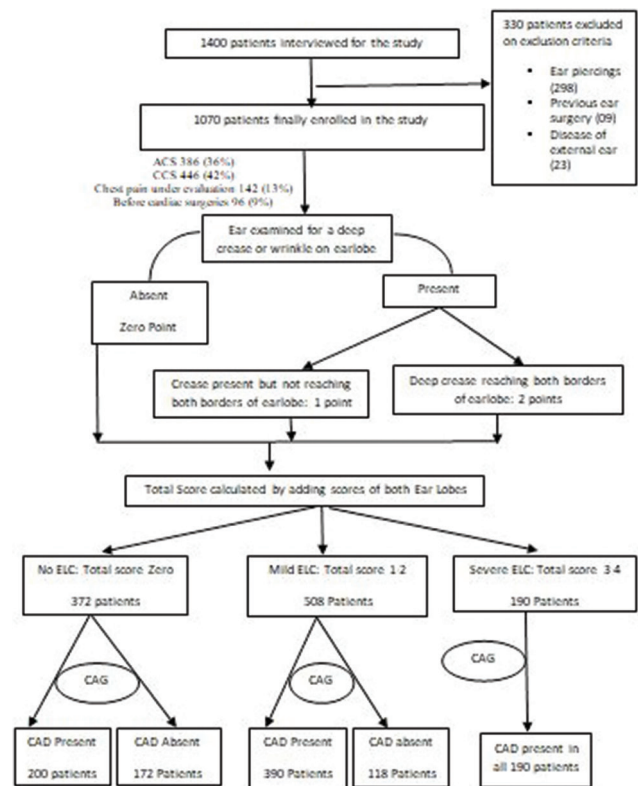


Figure 1: Flowchart depicting the methodology of the study. CAD = Coronary artery disease, CAG = Coronary angiography, ELC = Earlobe crease, ACS = Acute coronary syndrome, CSA = Chronic stable angina

association of physicians in India published in 2016.^[23] History of premature cardiovascular was defined as the onset of CAD before 55 years in males and 65 years in females.^[24] Tobacco consumption whether in the form of cigarette smoking or oral tobacco consumption was clubbed together as one and has been mentioned as smoking in the study.

Coronary angiogram

After informed consent, all the patients ($n = 1070$) underwent CAG (either by femoral, conventional radial, or dorsal radial approach) as per appropriateness use criteria published by ACC in 2017.^[19] The indications for which these patients underwent coronary angiography are illustrated in Figure 1. CAD was defined as luminal stenosis of >50% in at least one epicardial arteries and classified according to the involvement of single-vessel disease (SVD), double-vessel disease, and multivessel disease (MVD). All these patients were treated accordingly to appropriate use criteria as defined by the ACC/AHA in 2017.^[19]

Statistical analysis

Statistical analyses were performed using the SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean \pm standard deviation, whereas categorical variables were depicted as numbers (percentages). Comparisons between the groups were done by Student's *t*-test for continuous variables and by Chi-square or Fisher's test for categorical variables. $P < 0.05$ was considered statistically significant.

RESULTS

Of total 1070 patients, enrolled in the study, 780 patients had CAD proven by coronary angiography. Of these, 74% (580/780) had an ELC either mild or severe. A comparative analysis of the presence and severity of CAD in the ELC-negative, mild ELC, and severe ELC groups was done and is illustrated in Figure 3.

Demographic comparison

The demographic characteristics of the patients with and without ELC are compared in Table 1. ELC-positive

patients were significantly older than the ELC-negative patients (57.14 years vs. 51.45 years, $P < 0.0001$). Similarly, mean height (162.42 cm vs. 161.23 cm, $P < 0.0001$) and mean weight (64.64 kg vs. 63.22 kg, $P < 0.0001$) of the ELC-positive patients were significantly higher than the ELC-negative patients. The patients with ELC had a significantly higher incidence of HTN (62.17% vs. 41.17%, $P < 0.05$), DM (35.38% vs. 17.47%, $P < 0.05$), hypercholesterolemia ($P < 0.05$), and serum creatinine values ($P < 0.05$). On the other hand, the prevalence of smoking ($P = 0.29$) and family history of premature cardiovascular death ($P = 0.61$) were similar in both the groups.

Prevalence of earlobe crease and its correlation with coronary artery disease

The prevalence of CAD was found to be significantly higher (OR: 4.22 [95% CI: 3.18–5.61], $P < 0.0001$) among the patients with ELC (580/698) in comparison to patients without ELC (200/372). In the ELC-negative group ($n = 200$) who had CAD, 141 (70.50%) had SVD, whereas 59 (29.50%) had MVD [Figure 3]. The prevalence of MVD was found to be significantly higher among the ELC-positive patients than ELC-negative patients (OR: 5.03 [95% CI: 3.61–6.90], $P < 0.0001$). Moreover, MVD was significantly more prevalent in patients (OR: 6.27 [95% CI: 4.23–9.29], $P < 0.0001$) in the severe ELC group (150/190) in comparison to the mild ELC group (190/508).

The observed sensitivity of the sign of ELC for diagnosis of CAD was 74%, the specificity was 59%, the positive predictive value was 83%, and the negative predictive value was 46%.

DISCUSSION

Prevalence of earlobe crease

Since the association between CAD and ELC was first reported by Frank in 1973, it has been an area of immense debate. The association between ELC and CAD has been confirmed in several studies across varied geographical distribution with the prevalence of ELC among CAD-positive patients ranging from 41% to 82%, as illustrated in Table 2.^[4-13,16-18] In

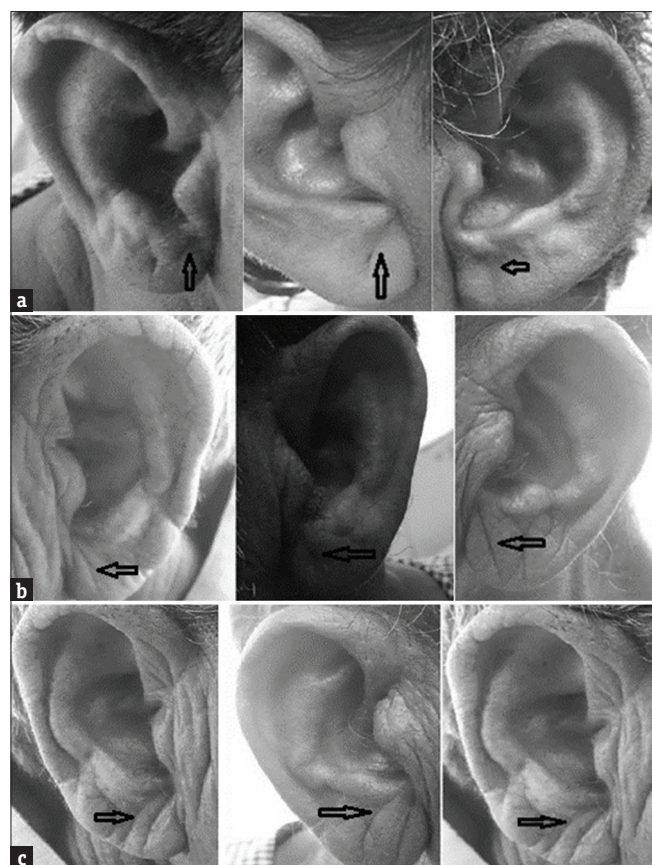


Figure 2: Types of earlobe creases

Table 1: Demographic comparison of patients with and without earlobe crease ($n=1070$)

| Demographic parameters | Mean (SD) | | MD (95% CI) | P |
|--------------------------|--------------------------------|-------------------------------|-------------------------|---------|
| | ELC present ($n=698$) | ELC absent ($n=372$) | | |
| Age (years) | 57.14 (13.42) | 51.45 (12.51) | -5.96 (-7.34--4.03) | <0.0001 |
| Weight (kg) | 64.64 (4.72) | 63.22 (4.25) | -1.42 (-1.99--0.84) | <0.0001 |
| Height (cm) | 162.42 (7.13) | 161.23 (7.31) | -99.20 (-100.10--98.29) | <0.0001 |
| Serum creatinine (mg/dl) | 1.22 (0.34) | 1.00 (0.32) | -0.22 (-0.26--0.17) | <0.0001 |
| Demographic parameters | ELC present ($n=698$), n (%) | ELC absent ($n=372$), n (%) | OR (95% CI) | P |
| Male sex | 510 (73.9) | 304 (81) | 1.04 (0.80-1.34) | 0.74 |
| Hypertension | 434 (62.17) | 154 (41.17) | 2.32 (1.80-3.00) | <0.0001 |
| Diabetes mellitus | 247 (35.38) | 65 (17.47) | 2.58 (1.89-3.52) | <0.0001 |
| Dyslipidemia | 407 (58.30) | 91 (24.46) | 4.31 (3.26-5.71) | <0.0001 |
| Smoking | 170 (24.35) | 80 (21.50) | 1.17 (0.86-1.58) | 0.29 |
| Family history of CAD | 94 (13.46) | 46 (12.36) | 1.10 (0.75-1.60) | 0.61 |

CAD=Coronary artery disease, CI=Confidence interval, ELC=Earlobe crease, MD=Mean difference, SD=Standard deviation, OR=Odds ratio

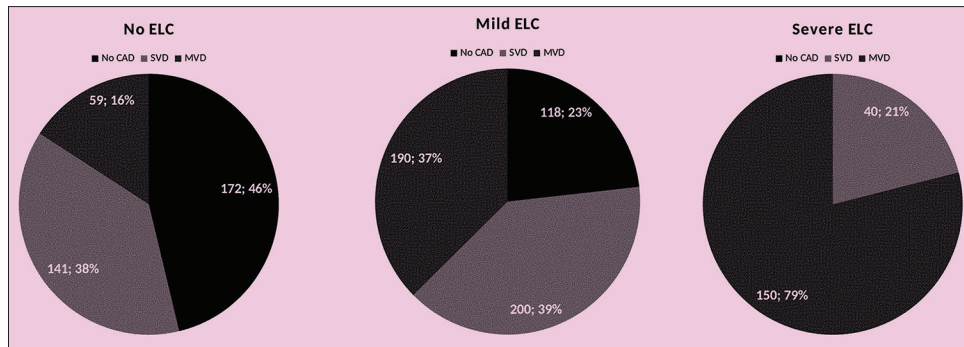


Figure 3: The distributions of coronary artery disease with respect to severity of earlobe crease. CAD = Coronary artery disease, ELC = Earlobe crease, SVD = Single-vessel disease, MVD = Multivessel disease

Table 2: Summary of significant studies evaluating earlobe crease as a risk factor for coronary artery disease

| Study (years) | Geographical location | Total patients screened (n) | CAG done | Prevalence of ELC in those with CAD (%) | Comments |
|--|-----------------------|-----------------------------|----------------|---|---|
| Verma <i>et al.</i> ^[18] | India | 215 | No | 47 | Patients with ELC more likely to have CAD |
| Evrengül <i>et al.</i> (2004) ^[4] | Turkey | 415 | Yes | 51.4 | Presence of bilateral ELC associated with increased risk of CAD (OR: 5.64 [95% CI: 3.37-9.45], $P<0.001$) |
| Edston ^[5] (2006) | Sweden | 520 | No | 55 | Based on autopsy studies (OR: 5.57 [95% CI: 3.81-8.14], $P<0.001$) |
| Raman <i>et al.</i> ^[17] | India | 1414 | No | 59.2 | Study included only known diabetics (OR: 0.88 [95% CI: 0.65-1.19], $P=0.004$) |
| Hou <i>et al.</i> ^[10] | China | 956 | Yes | 78 | Increased prevalence of risk factors in presence of ELC The study also evaluated prognosis after angioplasty and found that presence of ELC predicted a bad prognosis. (OR: 1.92 [95% CI: 1.37-2.66], $P<0.001$) |
| Shmilovich <i>et al.</i> ^[6] (2012) | USA | 430 | CT angiography | 71 | Patients with ELC more likely to have CAD (OR: 2.56 [95% CI: 1.81-3.30], $P<0.001$) |
| Suen <i>et al.</i> ^[13] | Hong Kong | 100 | Yes | 68 | Patients with ELC more likely to have CAD (OR: 1.02 [95% CI: 1.00-1.04], $P=0.04$) |
| Wu <i>et al.</i> ^[12] | China | 449 | Yes | 75.2 | Patients with ELC more likely to have CAD (OR: 3.40 [95% CI: 2.23-5.19], $P<0.001$) |
| Wang <i>et al.</i> ^[9] (2016) | China | 558 | Yes | 82 | Patients with ELC more likely to have CAD (OR: 4.86 [95% CI: 3.09-7.64], $P<0.001$) |
| Amit ^[16] | India | 255 | Yes | 41.2 | No difference in prevalence of risk factors in presence of ELC (OR: 2.18 [95% CI: 1.13-4.20], $P<0.001$) |
| Kamal <i>et al.</i> ^[11] (2017) | Pakistan | 200 | Yes | 41 | Patients with CAD more likely to have ELC (OR: 5.63 [95% CI: 2.91-10.93], $P<0.0001$) |

ELC=Earlobe crease, CAD=Coronary artery disease, CI=Confidence interval, ELC=Earlobe crease, SD=Standard deviation, OR=Odds ratio, CT=Computed tomography

our study, 74% of the patients of CAD proven on coronary angiography had an ELC. This finding is similar to the findings of the studies carried out by Wang *et al.* (82%),^[9] Hou *et al.* (78%),^[10] and Shmilovich *et al.* (71%).^[6] On the other hand, certain studies reported a lower prevalence of ELC in patients with CAD such as Kamal *et al.* (41%)^[11] and Evrengül *et al.* (51.45%).^[4] This could be explained by the smaller sample size or lower prevalence of CAD in the areas where these studies were carried out. In studies carried out in the Indian population, the reported prevalence of ELC in those with CAD was previously reported as 41.20% by Amit^[16] and 59.20% by Raman *et al.* (59.20%).^[17] This was a bit surprising

as contemporary studies carried out in China had reported a higher prevalence and could be due to a smaller sample size. Our study found that the prevalence was 74% which is in line with the recent contemporary studies.

Risk factors

This study was carried out in the Indian population and thus has a higher number of males than females attributable to the frequent ear piercings in Indian women. However, considering the pathophysiology involved, the result will most likely remain similar even among females. In our study, the ELC-positive patients were found to be

older in age and had a higher incidence of HTN, DM, hypercholesterolemia (please do not use capital letters for no reasons), and serum creatinine values, whereas the incidence of smoking and premature CAD did not show such a difference. This is similar to the findings reported by Hou *et al.*^[10] and Kamal *et al.*^[11] Both these studies reported an increased incidence of HTN and diabetes among those who had ELC when compared to those without ELC. They, however, did not report an increased incidence of hypercholesterolemia or serum creatinine values, as seen in our study. Other studies carried out earlier differed on this aspect. Amit (2016) reported no difference in the prevalence of risk factors, whereas other studies such as those by Shmilovich *et al.*,^[6] Edston,^[5] and Raman *et al.*^[17] did not include an assessment of the individual risk factors. The observation derived from our study is temporally correct in a sense that if the presence of ELC suggests an increased chance of CAD, then it should also be associated with increased prevalence of the risk factors known to cause CAD. The lack of an increased incidence of premature CAD could be because many patients were not well educated or aware about the disease in their family. In our study, higher body weight and height have been associated with the presence of ELC, which is corroborative of association of higher body mass index (BMI) to the presence of ELC in studies by Aligisaki *et al.*^[25] and Bawaskar *et al.*^[26]

Correlation with coronary artery disease

Our study demonstrated that patients with the presence of ELC had a higher incidence of CAD as confirmed by CAG, and the OR was found to be 4.22. This is in consistency with many previous studies, as illustrated in Table 2 which summarizes the findings of the recent studies carried out on this subject. The studies carried out in the Indian population by Verma *et al.*^[18] and Amit also confirmed the same observation. We also compared the type of CAD between those patients who did not have ELC with those who had ELC and found that those with ELC had a significantly higher risk of having multivessel CAD than those without ELC. Further, we also found that those who had severe ELC are more likely to have MVD than those with mild ELC. Similar observations were also made by Amit,^[16] Wang *et al.*,^[9] Hou *et al.*,^[10] Li *et al.*,^[12] and Lorna *et al.*^[13] Thus, it can also be concluded that increasing severity of ELC as assessed by the depth and length of the crease correlates with increasing severity of CAD. In fact, those patients of the 190 patients who had severe ELC all of them suffered from CAD, and a majority of them had MVD.

Limitations

The strength of this study lies in the fact that we used objective parameters like angiographic confirmation of CAD unlike many previous studies which used clinical definitions of CAD. However, the study was crosssectional in nature. The study was carried out in the cardiology department of a tertiary care teaching hospitals and may not reflect the prevalence or correlation in the general population. In our study, 65% of the total patients (580/1070) had ELC which may not be directive of regional or national prevalence.

CONCLUSION

ELC is an important clinical sign which should be examined carefully for its presence as well as severity. Both presence and severity of crease were related to occurrence and severity of CAD, respectively, in our study. Long-term cohort studies involving multiple ethnicity populations are necessary to determine the role of ELC in development as well as prognosis of CAD.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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