# Evaluation of diagonal earlobe crease (Frank's sign) as a non-invasive marker of cardiovascular diseases

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**Abstract:** *Background:* Cardiovascular diseases are the leading cause of death worldwide. Efforts for early diagnosis of cardiovascular diseases have compelled many clinicians to look for simple and non-invasive markers like diagonal ear lobe crease. *Objectives:* The aim of this study is to identify the prevalence of DELC and to determine the association of diagonal earlobe crease (DELC) with cardiovascular diseases. *Methods:* This was a case-control study conducted on two hundred participants in a tertiary care hospital. The participants were examined for the presence of DELC on both the ears and the severity of the crease was assessed. *Results:* The prevalence of DELC was 72% in cases and 17% in controls. Statistically significant association was found between DELC and cardiovascular diseases (P<0.0001).The sensitivity and specificity for DELC to predict cardiovascular diseases was 72% and 83% respectively. The odds of development of cardiovascular diseases in an individual with DELC (both unilateral and bilateral) was 12.55 times greater than an individual without DELC. *Conclusion:* DELC can be used as a simple and feasible screening tool for early diagnosis and prevention of cardiovascular diseases.

**Keywords**: Cardiovascular Disease, Diagonal Earlobe Crease, Frank's Sign.

## Introduction

Cardiovascular diseases are the leading cause of death worldwide, claiming nearly 17.9 Million lives every year and their prevention is a public health priority. Efforts to reduce the mortality through early diagnosis have compelled many clinicians to explore for simple and non-invasive markers [1]. Despite dramatic advances in diagnostic technologies, physical signs such as xanthelasma, arcus cornea and facial wrinkles are useful indicators of underlying disease. Just like acanthosisnigricans, DELC could be one of the dermatological manifestations of internal disease. Presence of frank's sign correlates with a myriad of cardiovascular diseases such as coronary artery disease, cerebrovascular disease & peripheral vascular disease [2].

It is also correlated to other risk factors like hypertension, hyperlipidemia, occipital baldness and with increased intima media thickness [3]. DELC is consideredas a surrogate marker which can identify patients with occult atherosclerosis [4]. Preliminary observations done by ancient Chinese traditional doctors revealed that a 'positive earlobe crease' is associated with development of premature coronary artery atherosclerosis [5].
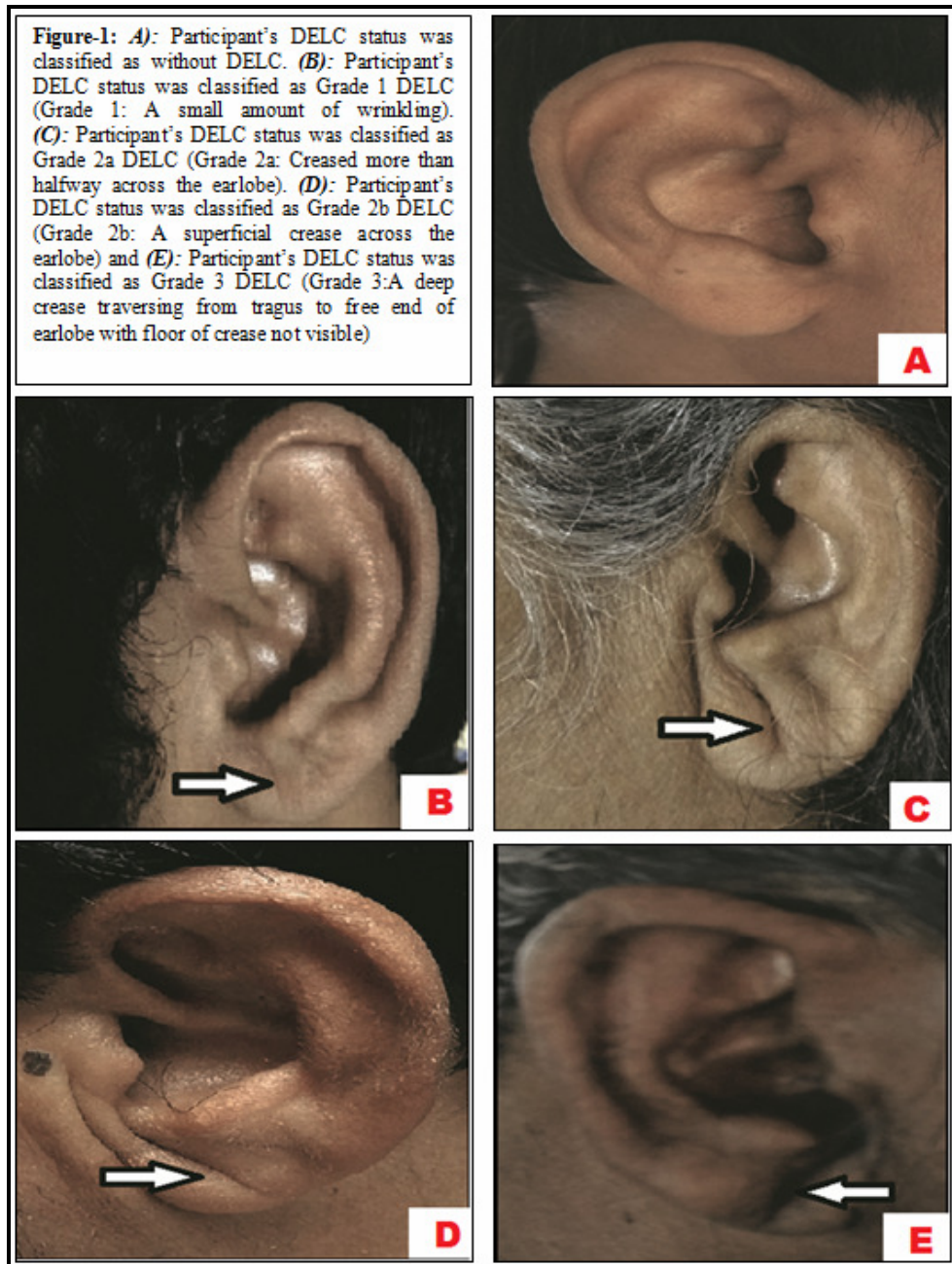
Diagonal earlobe crease was reported by Sanders T.Frank in 1973 and is named after him as Frank's sign. It is a diagonal crease in the earlobe extending from the tragus across the lobule to the rear edge of auricle [6]. It is associated with the carotid intima media thickness, which is a marker of subclinical atherosclerosis. It is also associated with the extent and severity of coronary artery disease (CAD), independent of traditional CAD risk factors, such as serum lipids, diabetes mellitus (DM) and smoking status. Presence of DELC is also correlated with ischemic stroke [7].

It was postulated that any pathological condition influencing microvasculature such as coronary artery disease, hypertension leads to development of DELC.Moreover, diffuse arrangement of elastic fibres was observed in

biopsy specimens from DELC, which resembled the morphology present in pathogenic heart [1]. Frank's sign is classified based on length, depth, bilateralism and inclination [8]. Highly extensive creases are more ominous than less extensive creases. The severity of the crease is graded [9] (Table-1 and Figure-1).

| Table-1: Grading of Frank's sign | |
|---|---|
| **Grade** | **Earlobe findings** |
| Grade 1 | A small amount of wrinkling on the earlobe |
| Grade 2a | Creased more than halfway across the lobe of the ear |
| Grade 2b | A superficial crease across the earlobe |
| Grade 3 | A deep crease traversing from tragus to free end of earlobe with floor of crease not visible |



Figure-1: *A)*: Participant's DELC status was classified as without DELC. *(B)*: Participant's DELC status was classified as Grade 1 DELC (Grade 1: A small amount of wrinkling). *(C)*: Participant's DELC status was classified as Grade 2a DELC (Grade 2a: Creased more than halfway across the earlobe). *(D)*: Participant's DELC status was classified as Grade 2b DELC (Grade 2b: A superficial crease across the earlobe) and *(E)*: Participant's DELC status was classified as Grade 3 DELC (Grade 3:A deep crease traversing from tragus to free end of earlobe with floor of crease not visible)

## Material and Methods

This was a case-control study conducted on 200 participants aged between 25-75 years at a tertiary care hospital, including 100 patients with documented cardiovascular disease and 100 controls. Patients were enrolled from the cardiology unit of the hospital with proven cardiovascular diseases. Control group were recruited from the surgical and medical units of the hospital who had no previously established evidence/symptoms of cardiac diseases such as dyspnoea on exertion & chest pain. Participants with external ear deformities, surgical scars and traumatic scars on the auricle were excluded from this study. Ethical clearance was obtained from institutional ethical clearance committee prior to start of the study. Informed consent was taken from each participant prior to data collection.

*Data collection:* Participants were examined for the presence of DELC on the lobular portion of either auricles. Participants were made to sit upright on bed; both ears were exposed and examined in adequate light. The presence of DELC is defined as deep crease /wrinkle present on earlobe, running from the lower pole of external meatus diagonally backward to edge of lobe at approximately 45 degrees without discontinuity covering 2/3rd of its path. Photographs of both the ears were taken. Presence of the crease on both the ears was documented as bilateral and presence of the crease on any one of the ears was considered as unilateral. Data regarding the demographic and clinical characteristics like age, gender, diabetes mellitus and smoking habits was collected.

Participants were documented as diabetics if they were on insulin or an oral hypoglycaemic medication.

*Statistical analysis:* Statistical analysis was done by using SPSS (statistical package for the social sciences) software. Comparison of the categorical or numeric variables between groups was carried out using Chi-square test. P-value of <0.05 was regarded as being statistically significant. Prevalence, odds ratio, sensitivity, specificity and predictive values of DELC among the participants were also computed.

## Results

A total of 200 participants were included in the study and the participants were divided into 2 groups. Each group comprising of 100 participants. Group I, comprising of 100 patients with cardiovascular diseases and Group II, comprising of 100 controls. Among the 200 participants, 113 were males and 87 were females. The mean age and standard deviation was 49.49 ± 14.48 years. Total participants (Patients and controls) were classified into five age groups (25-35, 36-45, 46-55, 56-65 and 66-75 years).

*Group I with Cardiovascular diseases:* Among the 100 patients in group I, unilateral crease was present in 17 individuals and bilateral crease was present in 55 individuals. The prevalence of DELC was 72% among cases and 17% among controls which was statistically significant (P<0.0001)(Table-2).

| Table-2: Comparison between cases and controls in relation to DELC | | | | | |
|---|---|---|---|---|---|
| **Participants** | | **DELC present** | | **DELC absent** | **Total** |
| | | **Unilateral** | **Bilateral** | | |
| Cases | Number(n) | 17 | 55 | 28 | 100 |
| | Percentage (%) | 17% | 55% | 28% | |
| Controls | Number(n) | 8 | 9 | 83 | 100 |
| | Percentage (%) | 8% | 9% | 83% | |
| | *P*-Value | <0.001 | <0.0001 | | |
| | Odds ratio | 6.29 | 18.12 | | |
| | 95% CI | 2.45-16.18 | 7.94-41.33 | | |

The odds of development of cardiovascular diseases in an individual with DELC (both unilateral and bilateral) was 12.55(95% confidence interval: 6.36-24.79) times greater than an individual without DELC. It was also observed that bilateral creases are more prevalent among the cases (Graph.1). The sensitivity and specificity for DELC to predict cardiovascular diseases was 72% and 83% respectively whereas the positive predictive value was 80.8% and the negative predictive value was 74.7%. Maximum number of individuals suffering with cardiovascular diseases had DELC of grade 1 and 2a (Table-3).

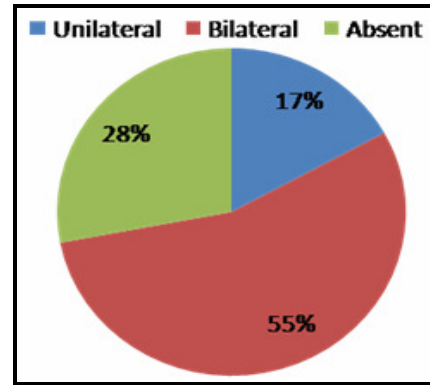**Graph-1:** Correlation of laterality of crease with cardiovascular diseases



### Table-3: Grade and age wise distribution of persons with DELC among cases.

| DELC | Age groups (years) | | | | | Total n ( % | p value |
|------|---------|---------|---------|---------|---------|---------|---------|
| | 25-35 n ( %) | 36 -45 n ( %) | 46-55 n ( %) | 56-65 n ( %) | 66-75 n ( %) | | |
| Grade 1 | 1(100) | 2(50) | 7(58.33) | 12(34.28) | 1(5) | 23(31.94) | 0.02 |
| Grade 2a | 0 | 1(25) | 3(25) | 11(31.42) | 5(25) | 20(27.77) | |
| Grade 2b | 0 | 1(25) | 2(16.67) | 7(20) | 6(30) | 16(22.22) | |
| Grade 3 | 0 | 0 | 0 | 5(14.28) | 8(40) | 13(18.05) | |
| Total | 1 | 4 | 12 | 35 | 20 | 72 | |

*Age:* It was observed that among the participants, the highest prevalence of DELC was seen in individuals between 56 to 65 years of age (Graph-2 and 3). There was a significant correlation between the presence of DELC and advanced age (P<0.001) (Table-4 and 5).

**Graph-2:** Age wise distribution of persons with and without diagonal earlobe crease among cases
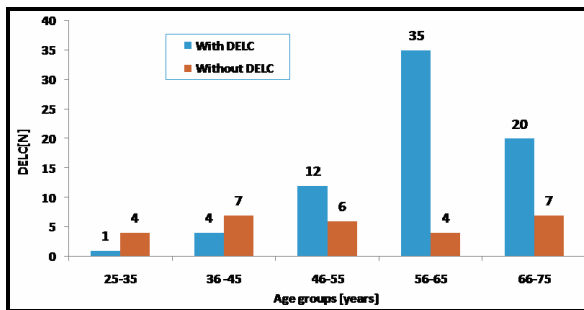


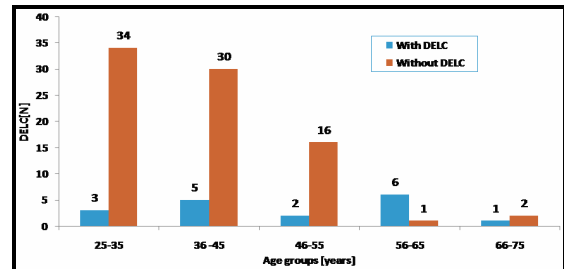**Graph-3:** Age wise distribution of persons with and without diagonal earlobe crease among controls



### Table-4: Age wise distribution of persons with and without DELC among cases.

| DELC | Age groups(years) | | | | | Total n ( %) | P-value |
|------|---------|---------|---------|---------|---------|---------|---------|
| | 25-35 n ( %) | 36 -45 n ( %) | 46-55 n ( %) | 56-65 n ( %) | 66-75 N( %) | | |
| Yes | 1 (20) | 4 (36.36) | 12 (66.66) | 35(89.74) | 20(74.07) | 72 (72) | <0.001 |
| No | 4 (80) | 7 (63.63) | 6 (33.33) | 4(10.25) | 7 (25.92) | 28 (28) | |
| Total | 5 | 11 | 18 | 39 | 27 | 100 | |

| Table-5: Age wise distribution of persons with and without DELC among controls. | | | | | | | |
|---|---|---|---|---|---|---|---|
| **DELC** | **Age groups (years)** | | | | | **Total** *n ( %)* | **P value** |
| | **25-35** *n ( %)* | **36 -45** *n ( %)* | **46-55** *n ( %)* | **56-65** *n ( %)* | **66-75** *n ( %)* | | |
| Yes | 3(8.10) | 5(14.28) | 2(11.11) | 6(85.71) | 1(33.33) | 17(17) | 0.01 |
| No | 34(91.89) | 30(85.71) | 16(88.88) | 1(14.28) | 2(66.66) | 83(83) | |
| Total | 37 | 35 | 18 | 7 | 3 | 100 | |

*Gender:* There was no gender difference. Among the 113 males, DELC was present in 54 males (48%) and out of 87 females, DELC was present in 35 females (40%).There was no significant association found between gender and DELC (Table-6 and 7).

| Table-6: Comparison of demographic and clinical characteristics among cases between subjects with and without DELC | | | | | |
|---|---|---|---|---|---|
| **Variables** | **Categories** | **DELC** | | **DELC absence** *n ( %)* | **Total** |
| | | **Unilateral** *n ( %)* | **Bilateral** *n ( %)* | | |
| Gender | Male | 10(16.66) | 32(53.33) | 18(30) | 60 |
| | Female | 7(17.5) | 23(57.5) | 10(25) | 40 |
| Smoking | Smoker | 7(20) | 21(60) | 7(20) | 35 |
| | Non-smoker | 10(15.38) | 34(52.30) | 21(32.30) | 65 |
| Diabetes mellitus | Present | 7(14.89) | 27(57.44) | 13(27.65) | 47 |
| | Absent | 15(28.3) | 10(18.86) | 28(52.83) | 53 |

| Table-7: Comparison of demographic and clinical characteristics among controls between subjects with and without DELC | | | | |
|---|---|---|---|---|
| **Variables** | **Categories** | **DELC present** *n ( %)* | **DELC absent** *n ( %)* | **Total** |
| Gender | Male | 12(22.64) | 41(77.35) | 53 |
| | Female | 5(10.63) | 42(89.36) | 47 |
| Smoking | Smoker | 4(28.57) | 10(71.42) | 14 |
| | Non-smoker | 13(15.11) | 73(84.88) | 86 |
| Diabetes mellitus | Present | 3(37.5) | 5(62.5) | 8 |
| | Absent | 14(15.21) | 78(84.78) | 92 |

*Classical coronary risk factors(DM and smoking):*It was observed that out of 55 diabetic patients, DELC was present in 37 individuals (67%) and among the 49 smokers, DELC was present in 32 individuals(65%).However, due to the smaller sample size, we were unable to establish statistical significance to these results(Table-6 and 7).

## Discussion

Considering the first report on association of frank's sign with coronary artery disease given by Sanders T. Frank in 1973 [6], many clinical, angiographic and post-mortem studies have been done. These studies revealed that there was a significant association between DELC and cardiovascular diseases and also suggested that it can be used

as a surrogate marker for identifying patients with cardiovascular diseases. However this association between DELC and cardiovascular diseases remained disputable till now due to its confounding effects on age, sex and different parameters used for diagnosis of cardiovascular diseases [9]. Some studies have attributed the presence of DELC as a sign of ageing and being overweight [3]. This brings up the need to conduct further studies in this field to reach a broader consensus towards this significant association.

*Pathophysiology of frank's sign:* In the early 1970s, it was suggested that the frank's sign was due to the poor blood supply in the arteries supplying the earlobes. A study conducted by Shoenfeld *et al*. revealed that diffuse arrangement of elastic fibres was seen in biopsy specimens from DELC, which is the similar morphology present in diseased heart [10]. A study conducted on Japanese population with metabolic syndrome found that DELC was associated with telomere shortening, which is an indicator for accelerated aging and associated atherosclerosis [11].

Kaukola in 1978, in a study conducted in Finland reported the correlation between DELC and cardiovascular diseases and concluded that the prevalence rate of DELC was significantly greater among the patients sustaining an acute myocardial infarction than among the controls [12]. A British forensic necropsy study concluded that men with DELC had 1.55 times higher risk of attaining cardiovascular cause of death than those without crease [13].More recent reports using B mode ultrasound have also linked DELC to atherosclerosis of the carotid artery [14].

Elliot and karrison conducted a prospective cohort study and found a positive association between frank's sign and all cause morbidity and mortality including cardiac cause[15]. A cross-sectional study conducted on 255 Indian patients suffering with coronary artery disease had revealed a significant association of DELC with coronary artery disease and the prevalence of DELC was statistically related to hypertension and smoking, whereas diabetes had no significant association with DELC [16].

In our study, we confirmed a positive association of earlobe crease with cardiovascular diseases and the presence of bilateral DELC was more prevalent in the patients with cardiovascular diseases.

## Conclusion

This study revealed that there was a significant association between DELC and cardiovascular diseases. The odds of development of cardiovascular diseases in an individual with DELC (unilateral or bilateral) was 12.55 times greater than an individual without DELC. Therefore, DELC can be used as a visual cutaneous clinical marker or as a screening tool for early diagnosis of cardiovascular diseases. It can aid the clinician in cardiac risk assessment and for identification of individuals requiring further evaluation whose prognosis can be improved by early preventive measures. More prospective cohort studies are needed to confirm this association.

**Conflicts of interest:** There are no conflicts of interest.

## References

1. Kamal R, Kausar K, Qavi AH, Minto MH, Ilyas F, Assad S, Shah SU. Diagonal earlobe crease as a significant marker for coronary artery disease: a case-control study. *Cureus.* 2017; 9(2):e1013.
2. Lin AN, Lin K, Kyaw H, Abboud J. A Myth Still Needs to be Clarified: A Case Report of the Frank's Sign. *Cureus.* 2018; 10(1):e2080.
3. Bawaskar HS, Bawaskar PH, Bawaskar PH. Diagonal ear lobe crease: A premonitory diagnostic sign of impeding ischemic heart disease. *Journal of Family Medicine and Primary Care,* 2018; 7(6):1361.
4. Friedlander AH, López-López J, Velasco-Ortega E. Diagonal ear lobe crease and atherosclerosis: a review of the medical literature and dental

implications. *Med Oral Patol Oral Cir Bucal.* 2012; 17(1):e153.

5. Wang Y, Mao LH, Jia EZ, Li ZY, Ding XQ, Ge PC, Liu Z, Zhu TB, Wang LS, Li CJ, Ma WZ. Relationship between diagonal earlobe creases and coronary artery disease as determined via angiography. *BMJ,* 2016; 6(2):e008558.

6. Frank ST. Aural sign of coronary-artery disease. *The New England Journal of Medicine,* 1973; 289(6):327.

7. Qamar A, Ioannides KL, Khetarpal SA, Kiss D. Bilateral earlobe creases and coronary artery disease. *Circulation,* 2014; 130(1):92-93.

8. Lee KG. Frank's sign–a dermatological link to coronary artery. *Med J Malaysia,* 2017; 72(3):195.

9. Kadam YR, Shah YM, Kore P. Diagonal earlobe crease: Prevalence and association with medical ailments. *Journal of Clinical and Preventive Cardiology,* 2018; 7(2):49.

10. Shoenfeld Y, Mor R, Weinberger A, Avidor I, Pinkhas J. Diagonal ear lobe crease and coronary risk factors. *Journal of the American Geriatrics Society,* 1980; 28(4):184-187.

11. Higuchi Y, Maeda T, Guan JZ, Oyama J, Sugano M, Makino N. Diagonal earlobe crease are associated with shorter telomere in male Japanese patients with metabolic syndrome. *Circulation Journal,* 2009; 73(2):274-279.

12. Kaukola S. The diagonal ear-lobe crease, a physical sign associated with coronary heart disease. *Actamedica Scandinavica, Supplementum.* 1978; 619:1-49.

13. Kirkham N, Murrells T, Melcher DH, Morrison EA. Diagonal earlobe creases and fatal cardiovascular disease: a necropsy study. *Heart.* 1989; 61(4):361-364.

14. Çelik Ş, Erdoğan T, Gedikli Ö, Kırış A, Erem C. Diagonal ear-lobe crease is associated with carotid intima-media thickness in subjects free of clinical cardiovascular disease. *Atherosclerosis,* 2007; 192(2):428-431.

15. Elliott WJ, Karrison T. Increased all-cause and cardiac morbidity and mortality associated with the diagonal earlobe crease: a prospective cohort study. *The American Journal of Medicine.* 1991; 91(3):247-254.

16. Kumar A. Frank's sign and coronary artery disease in Indian population. *Heart India,* 2016; 4(4):129.

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