Scholars Journal of Dental Sciences

OPEN ACCESS

Abbreviated Key Title: Sch J Dent Sci
ISSN 2394-4951 (Print) | ISSN 2394-496X (Online)
Journal homepage: https://saspublishers.com

Frank's Sign which is a Marker of Coronary Heart Disease

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DOI: https://doi.org/10.36347/sjds.2024.v11i08.002 | **Received:** 02.09.2024 | **Accepted:** 09.10.2024 | **Published:** 11.10.2024

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Abstract **Review Article**

In today's clinical practice, the importance of a thorough clinical examination of the patient is emphasised in the article. There are 2 real-world instances of diagonal earlobe creases, commonly referred to as Frank's sign. The patients in both cases have ischemic heart disease, however they differ in terms of age and Frank's sign severity. Data from the literature are presented regarding the frequency of Frank's disease in various population groups, as well as its clinical importance and potential underlying pathophysiological causes. In the medical literature, the diagonal ear lobe crease (DELC) is termed as a substitute sign that can detect high-risk individuals with hidden atherosclerosis. However, there hasn't been any research on this subject in the dentistry or medical literature. Most clinical, angiography, and postmortem data are in favour of the idea that DELC is a useful extravascular physical marker that can determine individuals who are at risk of dying from coronary artery atherosclerosis. Some research findings have failed to support the theory linking DELC to certain health conditions. However, recent studies utilizing B mode ultrasonography have indicated a connection between DELC and the development of carotid artery atherosclerosis. Another study has also associated DELC with the existence of calcified carotid artery atheromas visible on panoramic radiographs. Notably, DELC is highly noticeable on head and neck oncology screening examinations. When the patient's vital signs, medical examination, and panoramic radiograph are combined, the results are DELC can aid to assess the patient's risk of atherosclerosis.

Keywords: Frank'sign, Diagonal Earlobe Crease [DELC], Calcified carotid artery atheromas, High risk.

INTRODUCTION AND BACKGROUND

As the leading cause of mortality globally, coronary heart disease (CHD) prevention is a major people health priority. Many doctors are searching for noninvasive disease markers as a result of their efforts to diagnose coronary heart disease as early as possible. Early detection of coronary artery disease is crucial for successful surgical treatments. Cardiovascular examinations are frequently employed as pre-operative techniques to identify CAD. The tests that are frequently performed include cardiac catheterization, exercise thallium imaging, ambulatory ECG, and exercise ECG. Nevertheless, in an emergency, these data might not be accessible, and there might not be enough time to check the patient for CAD (Kuri, M *et al*., 2001).

REVIEW

EAR AS INDICATOR

More than In the Yellow Emperor's Classics of Internal Medicine published 2000 years ago, the first Chinese medical text, the ear was first mentioned. According to the books, all meridians converge at the ear, and the ear is connected to all internal organs and sections of the human body. Due to the reactive nature of the ear, different physical characteristics may manifest on the auricle when a bodily condition is present. These characteristics include variances in edema, wrinkles, papule appearance, size, and shape (Kuri, M *et al*., 2001).

FRANK SIGN

The DELC, is thought as a dubious physical indicator for CAD incidence. DELC extends diagonally, at a 45-degree angle, from the external meatus's lowest pole, back to the lobe's margin.Frank was the first to

report in 1973 that DELC was linked to CAD. They called it the Frank sign (Kamal, R *et al*., 2017).

CORONARY HEART DISEASE EPIDEMIOLOGY IN INDIA

Globally, cardiovascular diseases—particularly coronary heart disease, or CVD have reached pandemic proportions. In India, CVD leaded to 17.5 million fatal worldwide in 2012. Over 75% of these fatalities happened in underdeveloped nations. Compared to developed nations, where CHD mortality is quickly dropping, in developing nations, it is rising. This rise, known as the epidemiological shift, is caused by urbanization, industrialization, and associated changes in lifestyle. Beginning in the early 20th century, this shift had an impact on the developed world, which included North America and Europe, and it expanded to emerging nations fifty years later (Gupta, R *et al*., 2016).

STAGES OF EPIDEMIOLOGIC TRANSITION

There are five phases to epidemiological transition: 1. A period of famines and plague, characterised by low mortality from CVD (<10%), high neonatal and childhood mortality, and malnutrition and infectious infections; 2. The era of receding pandemics, during which improved public health systems result in a drop in communicable disease mortality and the prominence of cardiovascular disease (CVD), accounting for 10%–35% of deaths; 3. In the age of degenerative and man-made diseases, cardiovascular disease (CVD) causes more deaths than communicable diseases, accounting for 35–65% of all deaths. 4. The age of delayed degenerative illnesses, in which CVDs and cancer account for more than 40% of all fatalities notwithstanding a downward trend in mortality rates; and 5. Age of obesity and inactivity, when a decrease in physical activity causes (Gupta, R *et al*., 2016).

CVD MORTALITY

The high CVD mortality rate in India and South Asia is caused by four reasons. These include:

a) Deficiency in social determinants of disease programmes aimed at reducing the use of alcohol, tobacco smoke, cigarettes, physical inactivity, and poor diets, which are fundamental risk factors;
b) Inadequate preventive care, which includes failing to control risk factors such as high hypertension, high cholesterol, and diabetes mellitus and obese
c) Inadequate acute care for congestive heart failure (CHD)
d) Inadequate long-term care for these patients, as well as the absence of cardiovascular rehabilitation and secondary prevention programmes. Regretfully, all of these elements are very common in India (Gupta, R *et al*., 2016).

GLOBAL BURDEN OF IHD MORTALITY:

As of February 2014, only 13 nations had provided 2012 ischemic heart disease (IHD) mortality data, with little over half of the countries submitting data since 2007. Twenty-four others provided data in prior years, while 79 nations, including China and India, have never submitted IHD data to the WHO despite their significant contribution to global IHD mortality. Resource limitations may explain delays in some countries like India, but wealthier nations like China and the UAE should face fewer challenges. Predictive methods for missing data exist but may introduce errors. Providing this data is crucial for assessing global health burdens and planning resources, as shown by timely submissions from countries like Moldova and Serbia (Nowbar, A. N *et al*., 2014).

RISK FACTORS

In India, no precise studies have determined the risk factors for coronary heart disease (CHD), but the INTERHEART study assessed key risk factors for early CHD. Eight prevalent variables accounted for over 90% of acute myocardial ischemia in South Asian and Indian patients. These include the apoprotein B-to-apoprotein A1 ratio, dyslipidemia, smoking, tobacco use, diabetes, hypertension, abdominal obesity, physical inactivity, an imbalanced diet, and psychological stress. According to World Health Statistics, these cardiovascular disease (CVD) risk factors are widespread in India: smoking and tobacco use affect 2.4% of men and 22.8% of women, obesity affects 3.2% of men and 6.7% of women, hypertension affects about 25% of the population, and diabetes affects roughly 10% (Gupta, R *et al*., 2016).

Unhealthy habits such as alcohol abuse, tobacco use, physical inactivity, and diets high in trans and saturated fats are also common. Nationally representative data are still needed, as most assessments are based on localized studies. However, a key trend is the faster rise of CVD risk factors in rural and slum populations compared to urban ones. While smoking is declining in educated urban areas, it is increasing in more literate rural areas. The adoption of labor-saving technologies in rural homes has contributed to sedentary lifestyles, while dietary habits have shifted toward high-calorie fast foods, both Indian and Western (Gupta, R *et al*., 2016).

Hypertension rates are now similar between urban and rural areas. Over the past two decades, urban hypertension rates have stabilized at 28%-32%, while rural rates have surged from 10%-12% in the 1990s to 22%-25%. Obesity is also rising faster in rural areas, serving as a proxy for increasing abdominal obesity and other cardiometabolic risk factors. These trends indicate that the CHD epidemic in India is likely to worsen in the coming years (Gupta, R *et al*., 2016).

A mean age of 51.5 years was observed in a study population where 2.6% had diabetes and 8.3% were on medication for hypertension. After excluding 9.9% (437/4418) of men who reported a medical diagnosis of heart attack, stroke, or angina, data from 2571 of 3981 men (aged 35-74) who participated in the 1998 Health Survey for England (HSE) were analyzed for coronary risk (64.6%) (Gupta, R *et al*., 2016).

RISK OF CORONARY ARTERY DISEASE IN MEN AND THE OVERWEIGHT AND OBESITY EPIDEMIC

Coronary Risk

The study's risk equations indicated a median projected 10-year coronary artery disease (CAD) risk of 11.6 per 100 men. CHD risk was associated with income and education level but not social status. Among lifestyle factors, physical activity and smoking were significant, while fat or fiber consumption was not. Body mass index (BMI) and waist-to-hip ratio (WHR) showed the strongest links to CHD risk (Nanchahal, K *et al*., 2005).

High Coronary Risk

About one-third of men had a 10-year CHD risk of ≥15%. This risk was significantly linked to income, smoking, physical activity, BMI, WHR, and education level. Within BMI groups, the occurrence of high risk increased with rising WHR, though less so at high WHR values.

Risk Contributable to Population:

BMI ≥25 kg/m² and WHR ≥0.95 accounted for 32% of high-risk cases. In this sample, 59.3% to 78% of men had a 10-year CHD risk of ≥15%. If men lowered their BMI and WHR below these thresholds, the proportion of high-risk men could drop by 46.6%. Income, education, smoking, and inactivity contributed an additional 31.4% to high-risk cases (Nanchahal, K *et al*., 2005).

BMI and WHR

Among 2440 men, 26% had a BMI <25 kg/m² and WHR <0.95. Obesity was less common among smokers, but WHR had a stronger link to income, physical activity, and education than BMI. WHR ≥0.95 was more common as wealth and education decreased and physical inactivity rose, particularly among smokers.

Age-Modified Occurrence of Increased BMI and WHR

Cholesterol and systolic blood pressure increased rapidly with rising BMI when WHR was <0.95 but remained high across all BMI levels for men with WHR ≥0.95. HDL-cholesterol decreased with rising BMI, especially in men with WHR ≥0.95 (Pasternac, A *et al*., 2007).

IS THE EXISTENCE OF DIAGONAL EAR LOBE CREASE LINKED TO DIABETIC RETINOPATHY IN THE SOUTH INDIAN DIABETIC POPULATION?

Clinical assessments of diabetic retinopathy were conducted using the Adapted Early Management of Diabetic Retinopathy Study criteria and the Airlie House Classification system. Retinal images were taken after pupil dilation with a Carl Zeiss Fundus Camera, using 45° 4-field stereoscopic photography. There was significant agreement (k = 0.83) between two independent assessors evaluating the images. "Sight-threatening diabetic retinopathy" included proliferative and non-proliferative retinopathy and macular edema. The diagonal ear lobe crease (ELC) has been linked to vascular disease, but its association with diabetic retinopathy is uncertain. Univariate analysis showed a slight correlation between ELC and sight-threatening retinopathy. However, multivariate analysis found the link insignificant, and ELC's predictive value for diabetic retinopathy was low, making it an unreliable screening marker. ELC affects about 60% of diabetic urban South Indians over 40 (Raman, R *et al*., 2009).

A SEPARATE RISK FACTOR IN CORONARY HEART DISEASE: DIAGONAL EAR-LOBE CREASE?

This study, conducted in December 1979, investigated the potential link between diagonal ear-lobe creases (ELC) and myocardial infarction (MI). Twenty-three MI patients from two hospitals were compared with 23 control patients, matched by age and gender, who had no history of heart disease. ELC was present in 17 MI patients and 20 control patients. A chi-square test showed no significant association between ELC and MI (P = 0.55). While the idea of ELC as a visual marker for coronary heart disease is interesting, this study found no strong evidence supporting its role as an independent risk factor (Farrell, R. P *et al*., 2018).

FRANK'S SIGN ASSOCIATED WITH ATHEROSCLEROTIC ALTERATIONS IN CAROTID BLOOD VESSELS

The study assessed the presence of the diagonal ear-lobe crease (DELC) and its association with carotid artery atherosclerosis. Patients' ear lobes were manually examined for DELC, defined as a deep diagonal line running from the tragus to the lobe's edge, covering at least two-thirds of the lobe's length. One patient displayed a typical DELC. Carotid artery intima-media thickness (IMT) and plaque scores (PS) were measured. The DELC-present group showed higher PS and plaque numbers (PN) compared to controls, with 48% of the DELC group exhibiting moderate-to-severe atherosclerotic changes versus 27% in the control group. This suggests an association between DELC and increased atherosclerosis (Shrestha, I. *et al*., 2009).

ASSOCIATION BETWEEN CORONARY ARTERY DISEASE AS IDENTIFIED BY ANGIOGRAPHY AND DIAGONAL EARLOBE CREASES:

This study involved 558 Chinese patients (402 men, 156 women) aged 36 to 91, who underwent coronary angiography at Nanjing Medical University to assess the link between diagonal ear-lobe creases (DELC) and coronary heart disease (CHD). DELCs were classified as unilateral or bilateral based on their depth and length, and coronary atherosclerosis was evaluated using the Gensini score. The study found a significant and independent correlation between DELC presence and higher CHD risk. Bilateral DELCs were associated with a greater relative risk of CHD compared to unilateral DELCs or no DELC. The research also highlighted strong positive associations between DELC, smoking status, age, and sex, all of which are related to CHD risk.

INFERENCE

The study's strength lies in its use of coronary angiography for diagnosing CHD and a standardized form for DELC evaluation. However, the small sample size, gender imbalance, and lack of exploration of the biological mechanism behind the DELC-CHD relationship were noted limitations. The findings suggest that DELCs, especially bilateral ones, could serve as a simple diagnostic marker for CHD, though further research is needed to confirm this link and understand its underlying causes (Yong, L *et al*., 2016).

AGE IS ASSOCIATED WITH EARLOBE CREASE, FRANK'S SIGN, AND ABNORMAL ANKLE-BRACHIAL INDEX MEASUREMENTS: A LITERATURE-BASED STUDY

The study followed the American Heart Association's guidelines for assessing Ankle-Brachial Index (ABI), measuring blood pressure using manual monitors and Doppler devices. ABI was calculated by comparing systolic blood pressure from the arms to that from the legs, with values <0.9 indicating peripheral artery disease (PAD) and values >1.4 suggesting calcinosis. The research evaluated confounding factors, including cholesterol levels and lifestyle habits.

INFERENCE

Findings suggested that the high prevalence of abnormal ABI in the elderly may obscure its relationship with diagonal ear-lobe crease (ELC), indicating that ELC is not a reliable marker for identifying individuals at risk for abnormal ABI results (Oscar, H *et al*., 2018).

THE SIGNIFICANCE OF DIAGONAL EARLOBES AS MARKERS OF CORONARY ARTERY DISEASE IN A POPULATION OF THE SALAHIDDIN PROVINCE IN IRAQ

The study confirmed that men become increasingly susceptible to coronary artery disease (CAD) after age 55, with testosterone reducing the effectiveness of lipoprotein lipase (LPL), resulting in elevated blood lipid levels and cholesterol. Patients exhibited a higher body mass index (BMI) compared to controls, aligning with findings from AL-Gebori *et al*., (2013). Diabetes and hypertension levels were also significantly elevated among patients, consistent with Khalaf's 2015 research, attributed to increased oxidative stress and free radicals. Cholesterol and triglyceride levels were notably higher in patients, while HDL levels were lower, corroborating findings from Heidari *et al*., (2013).

The study observed a 34.1% prevalence of diagonal ear-lobe crease (DELC) among patients, consistent with Edston *et al*., (2006), who reported a higher prevalence of DELC in northern European autopsies. Previous research has established a significant correlation between DELC and CAD, although the underlying pathophysiological mechanisms remain unclear. It is hypothesized that DELC may indicate subclinical atherosclerosis and shared genetic factors. This research is notable as it is the first to demonstrate a significant association between DELC and CAD identified through coronary angiography in Iraq, suggesting DELC could serve as a preliminary marker for CAD risk (Khalaf, O. R *et al*., 2018).

UPCOMING CORONARY ARTERY DISEASE

The presence of diagonal ear-lobe crease (DELC) is a significant external marker for ischemic heart disease (IHD). In females aged ≥50, the correlation with IHD has an odds ratio of 18.54, while in males over 50, it's 5.39. For individuals under 50, the odds ratio is 3.79, with hyperlipidemia at 6.35 and occipital alopecia at 7.49. Among the studied population, 57% had DELC, higher than the 47% found in New York's urban population. The study links DELC to IHD, hypertension, diabetes mellitus, hyperlipidemia, tobacco use, and occipital alopecia, suggesting that DELC can be used by nonclinicians in rural areas to identify individuals at high risk for IHD, particularly in underdeveloped nations like India (Himmatrao, S. N. *et al*., 2018).

Patient Consent Declaration

The practitioner confirm that they possess all required patient consent documentation. Patients have provided written consent for the publication of their photographs and other clinical data in the journal.

Patients are aware that their identity will be kept hidden, including the omission of their names and initials, but complete anonymity cannot be guaranteed (Himmatrao, S. N *et al*., 2018).

DENTAL CONSEQUENCE

In 2007, Celik *et al*., conducted the first study examining the association between diagonal earlobe crease (DELC) and carotid artery stenosis using B-mode ultrasound in a cohort of healthy Turkish volunteers. They focused on carotid intima-media thickness (CIMT), an essential indicator of atherosclerosis, discovering that participants with one or both sides of DELC exhibited

significantly higher CIMT compared to age- and sex-matched controls without DELC.

Building on this research, a 2009 study in Japan assessed 212 patients (106 males and 106 females, mean age 67) who required B-mode ultrasound for cardiovascular concerns. The study found that 30% of patients had DELC, which independently correlated with increased CIMT and was also associated with a higher number of atherosclerotic plaques and plaque scores. This suggests that DELC may have a more direct relationship with coronary artery atherosclerosis than CIMT itself.

In 2010, inspired by Celik's findings, a dental researcher published results on DELC in ten neurologically normal patients, all confirmed to have calcified carotid artery atheroma (CCAA) through dental radiographs and B-mode ultrasound. The findings emphasized the importance of dental practitioners screening for DELC during head and neck examinations, as this information, along with patients' medical histories and vital signs, can help assess risks for coronary and carotid artery diseases, guiding appropriate medical interventions and evaluations (Friedlander, A. H *et al*., 2012).

DIAGONAL EARLOBE CREASE: FREQUENCY AND RELATIONSHIP TO MEDICAL CONDITIONS

This case-control study investigates the relationship between Diagonal Earlobe Crease (DELC) and coronary artery disease (CAD), as well as other cardiovascular risk factors. The authors aimed to determine whether DELC could serve as an indicator of CAD, diabetes mellitus (DM), and hypertension (HTN), suggesting it reflects underlying atherosclerosis.

The study involved 168 participants, including 50 controls with no evidence of coronary heart disease (CHD) and 118 patients with confirmed CAD who underwent angiography. Data on participants' age, sex, medical history, blood pressure, lipid profiles, and smoking status were collected. DELC was assessed using a modified version of Shrestha's evaluation form, and patients were categorized by age groups (40–50, 51–60, 61–70, >70 years).

Results showed that DELC was strongly associated with CAD, particularly in older males and those with hypertension, but not with diabetes, hyperlipidemia, or smoking. DELC was found to have a sensitivity of 90% and a specificity of 52.51% in predicting CAD, with an overall accuracy of 72.62%. Logistic regression analysis confirmed that DELC is significantly correlated with CAD, even when adjusting for traditional cardiovascular risk factors.

The study's findings support the theory that DELC could predict generalized atherosclerosis and heart disease, though conflicting studies exist. Some research highlights the varying degrees of association between DELC and heart disease, likely influenced by differing diagnostic criteria and confounding factors like age and sex.

However, the study acknowledges its limitations, including its single-center design, small sample size, and focus on a specific ethnic group, which may affect the generalizability of its results. The authors recommend larger-scale longitudinal studies to further investigate the potential of DELC as a predictive marker for cardiovascular conditions (Ramdurg, P *et al*., 2018).

CONCLUSION

Most medical research supports a link between DELC and CHD, despite some conflicting findings. This study found a significantly higher prevalence of DELC in patients with CHD, indicating that DELC may serve as an independent risk factor for CAD. The correlation between DELC and primary coronary risk factors further supports this. DELC may be a useful and easily identifiable indicator in dental practices, aiding oral surgeons in assessing patients' risk levels. (Ramdurg, P *et al*., 2018).

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