



# Family history of sudden cardiac death among victims of sudden death in yazd, iran

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## Abstract

**Objectives:** A positive family history of Sudden Cardiac Death (SCD) is an independent risk factor for mortality. This study aimed to determine the prevalence of a positive family history of SCD and its associated risk factors among victims of sudden death in Yazd.

**Methods:** This cross-sectional study investigated SCD cases in Yazd, Iran, in 2011. The study included victims who were aged 20 years or older, and the cause of death was the cardiac arrest within one hour of symptom onset. The data obtained from families of SCD victims through verbal autopsy interviews.

**Results:** A total of 317 cases of SCD occurred among victims, resulting in an incidence rate of 139.4 per 100,000 population. 26.2% had a positive family history of SCD, with a mean age of  $60.4 \pm 12.3$  years. Individuals with a positive family history of SCD had a significantly younger mean age at the time of death ( $60.9 \pm 12.3$  vs.  $66.9 \pm 16.5$  years,  $P = 0.018$ ). The prevalence of diabetes mellitus (odds ratio 1.43, CI 95% = 1.03–1.99,  $P = 0.042$ ), dyslipidemia (odds ratio 1.47, CI 95% = 1.07–2.1,  $P = 0.038$ ), chronic coronary artery disease ( $P = 0.027$ ), and revascularization ( $P = 0.049$ ) had a significant association with positive family history of SCD.

**Conclusions:** This study highlights the importance of assessing family history as a risk factor for SCD, along with other risk factors such as diabetes, dyslipidemia, and chronic coronary artery disease.

**Keywords:** Sudden cardiac death, risk factor, family history, coronary artery disease

## Introduction

Sudden cardiac death (SCD) is a significant public health concern worldwide, with a substantial socioeconomic burden [1-3]. In the United States alone, the reported incidence of SCD is 450,000 cases per year, while the global incidence is estimated to be 4-5 million cases annually [4, 5]. SCD

accounts for half of all cardiovascular deaths, with the majority of cases caused by coronary artery disease [6, 7]. While most cases of sudden cardiac death are not hereditary, having a family history of SCD is a significant and independent risk factor for SCD in first-degree relatives. The prevalence of a family

history of sudden death in victims is 18.6%. The sudden death of one or both parents increases the relative risk of SCD by 1.8% and 9.4%, respectively. Recent statistics suggest that 12% of adults aged 20 years or older have a parent or sibling who experienced a heart attack or angina before the age of 50, predicting the risk of sudden death due to premature coronary atherosclerosis in these families [8-10]. A history of SCD can serve as a warning sign for investigating other family members for genetic syndromes or commonly acquired potentially fatal risk factors. This study was conducted in Yazd, an ancient city in Iran, to determine the prevalence of a family history of sudden death and its associated risk factors among sudden death victims in this region [11].

### Materials and Methods

The present cross-sectional study was conducted in Yazd, Iran to investigate sudden cardiac deaths (SCD) that occurred within a year and to examine the families of the victims. The study included individuals aged 20 or older who died of cardiac arrest within one hour of symptom onset. The study excluded deaths resulting from trauma, drug or non-drug poisoning, end-stage situations, chronic illness, and certain diseases. The Ethics Committee of Shahid Sadoughi University of Medical Sciences approved the study, and participants provided informed consent before being interviewed. The diagnosis of SCD was based on death certificates containing relevant International Classification of Diseases 10th Revision (ICD-10) codes. Additionally, the researchers conducted verbal autopsies with family members of cases of definite SCD. In cases where families were unavailable, the study relied solely on hospital death certificates and coroner records. The data collected included demographic information, past medical history of cardiovascular diseases, angiography and revascularization procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), history of coronary artery disease risk factors, and family history of SCD in first-degree relatives. The occurrence of SCD in an immediate relative was confirmed by reviewing their medical records, death certificate, or through the description of symptoms reported by the interviewed person.

### Statistical analysis

Data analysis was performed using SPSS version 19 (IBM Inc, NJ, USA). Continuous variables were presented as mean and standard deviation, while categorical variables were presented as percentages

and numbers. T-test and chi-square were used for continuous and categorical variables, respectively. In order to examine the connection between nominal variables, we employed Yates' correction and Crammer's coefficient. These methods were utilized to guarantee that the findings were not impacted by the sample size or the frequency of the data. A p-value of 0.05 or less was deemed statistically significant.

### Results

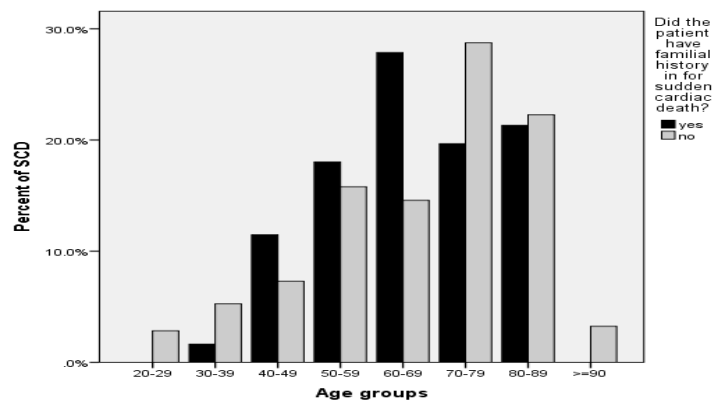
In Yazd, Iran, there were 317 instances of sudden death among residents who were 20 years and older in a total population of 227,367. The incidence of sudden cardiac death was 139.4 per 100,000 people. Out of all the cases, 73.8% (n=247) had no familial history, while 26.2% (n=83) had a positive family history of sudden cardiac death. The victims with a positive family history of SCD had a significantly younger mean age compared to those without a familial history of SCD (60.9 ±12.3 vs. 66.9 ±16.5 years,  $P= 0.018$ ). Overall, 23.2% of men and 30.1% of women among the 317 SCD cases had a familial history of SCD. In victims with a positive family history of sudden cardiac death, there was a significant incidence of SCD among those with diabetes mellitus ( $P = 0.042$ ), dyslipidemia ( $P = 0.038$ ), and prior revascularization ( $p = 0.049$ ). Although the prevalence of heart failure, hypertension, smoking, and prior myocardial infarction was higher in victims with a positive familial history of SCD, these differences were not statistically significant. The family history of SCD in immediate relatives of victims who experienced SCD before the age of 70 was events occurring one decade earlier than those without a family history of SCD in their first-degree relatives. Male victims with a positive family history of SCD in first-degree male family members (father or brothers) had a significant 1.5-fold increased incidence of SCD ( $P = 0.019$ ). Women with a family history of SCD in first-degree male family members (fathers or brothers) also showed an increased incidence of SCD, but the odds ratio was not significant. Victims with a positive family history of sudden cardiac death had a significantly higher frequency and increased odds of diabetes mellitus (OR = 1.43, 95% CI = 1.03–1.99) and dyslipidemia (OR = 1.47, 95% CI = 1.04–2.1). The prevalence of hypertension and ischemic heart disease was higher in female victims with a positive family history of sudden cardiac death who were under 60 years old, but the odds ratio was not significant.

**Table 1:** Characteristics of victims with and without a family history of sudden cardiac death

Variable	Positive FH n=83	Negative FH n=234	P-value
Age	60.9 ± 12.3	66.9 ± 16.5	0.018
Sex			
Male	42(50.6%)	139(59.4%)	0.164
Female	41(49.4%)	95(40.6%)	
Marital status			
Married	65(78.3%)	185(79.1%)	0.866
Single	1(1.2%)	7(3.0%)	0.373
Divorced	1(1.2%)	7(3.0%)	0.373
Widowed	16(19.3%)	35(15.0%)	0.357
Smoking	16(19.3%)	63(26.9%)	0.166
Hypertension	36(43.4%)	87(37.2%)	0.320
Diabetes Mellitus	34(41.0%)	70(29.9%)	0.042
Dyslipidemia	31(37.3%)	64(27.4%)	0.038
Chronic CAD	27(32.5%)	47(20.1%)	0.027
Acute MI	28(33.7%)	64(27.4%)	0.271
Revascularization (CABG/PC)	19(22.9%)	31(13.2%)	0.049
heart failure	5(6.1%)	12(5.1%)	0.756

**Table 2:** Prevalence of sudden cardiac death in first-degree relatives

First-degree relatives	Number (%)	Max age	Min age	Mean age
Father	22 (%25)	80	36	59.4
Mother	21 (%24)	90	47	64.5
Brother	19 (%22)	82	37	58.2
Sister	25 (%29)	80	27	56.4
Total	87	90	27	59.8



**Figure 1:** Comparison of the frequency of familial sudden cardiac death across age groups

**Table 3:** The odds ratios of different factors in Sudden Cardiac Death victims who have a family history of SCD are compared to those without such a history

Predictor	Odds Ratio	95% CI
Age $\geq$ 40	1.47	0.60- 3.65
Male gender	1.30	0.90– 1.88
Diabetes Mellitus	1.42	0.98– 2.06
Hypertension	1.21	0.83– 1.75
Hyperlipidemia	1.584	0.93– 2.69
Smoking	1.40	0.86– 2.28
Acute myocardial infarction	1.25	0.85– 1.83
Chronic CAD	1.58	1.07– 2.33
Revascularization	1.60	1.00– 2.56

## Discussion

The present study found that a significant proportion (26.2%) of sudden cardiac death (SCD) cases had a familial history of the condition, which is higher compared to the Paris prospective study. The result may be attributed to the high rate of consanguineous marriages in Yazd [11, 16].

Familial history of SCD was found to increase the risk of SCD, particularly in individuals under the age of 70, with a high prevalence of chronic or acute ischemic heart disease in victims with familial history. SCD is often the first manifestation of coronary artery disease (CAD) and is responsible for approximately 50% of cardiovascular disease mortality in developed countries [17-21].

Family history and genetic predisposition play crucial roles in cardiovascular disease and SCD, with

approximately 51% of heart diseases leading to SCD being hereditary [5, 18, 22, 23].

Our findings indicate that the total number of first-degree relatives who experience sudden cardiac death (SCD) is directly related to the risk of SCD in other family members, as seen in similar studies [3, 24, 25]. The study found that dyslipidemia and diabetes were significant predictors of SCD in victims with familial history, which is consistent with previous studies. Smoking, diabetes, and high blood pressure were also identified as predictors of SCD, with myocardial infarction (MI) being more prevalent in individuals with a familial history of SCD. About one-third of the victims had a history of acute myocardial infarction (AMI), and abnormal serum cholesterol concentrations, particularly an elevated ratio of total

cholesterol to high-density lipoprotein cholesterol (TC/HDL-c), in men with CAD who die suddenly, predispose patients to the rupture of vulnerable plaques. While genetic screening may not be feasible for all family members of SCD victims, it may help reduce the risk of subsequent death within a family [26-29].

While coronary revascularization aims to reduce mortality, including SCD, many patients with ischemic cardiomyopathy remain at risk of SCD [21, 30]. The present study found that victims with a history of familial SCD were more likely to have undergone coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). However, the study suggests that while revascularization may decrease the overall number of deaths, it may not reduce the proportion of SCDs in this specific group. It is therefore, essential to identify familial history and genetic predisposition to help reduce the risk of SCD in families and improve patient outcomes.

### Limitations of the study

Some limitations of the study include:

1. Selection bias: The study relied on death certificates from various sources, which may not have included all cases of sudden death in the region, which could result in an underestimation of sudden cardiac deaths and limit the generalizability of the findings.
2. Recall bias: The study used verbal autopsies to collect information on the cause of death for older death certificates, which could be subject to recall bias. Family members may not accurately remember the symptoms or events leading up their loved one to death, which could affect the classification of sudden cardiac death.
3. Inadequate risk factor information: The study failed to gather data on crucial risk factors for sudden cardiac death, like family history of cardiovascular diseases, physical activity, and smoking status. This omission could hinder accurate assessment of how familial history influences the risk of sudden cardiac death.
4. Restricted age range: The study solely involved participants aged 20 years and above, potentially not

reflecting the broader population. Sudden cardiac death can affect younger individuals, so excluding them may restrict insights into how familial history impacts the risk of sudden cardiac death across all age brackets.<sup>5</sup> Insufficient genetic testing: The research lacked genetic testing to pinpoint potential genetic variants linked to sudden cardiac death. This data is crucial for identifying individuals at high risk of sudden cardiac death and creating targeted prevention strategies.

### Conclusion

This study emphasizes the significant public health impact of SCD in Yazd, with a high incidence rate of 139.4 per 100,000 residents aged 20 years or older. Notably, a quarter of the victims had a positive family history of SCD, highlighting the importance of family history as a risk factor for this condition.

Interestingly, the study found that hypertension and smoking were not significantly associated with a family history of SCD. However, victims with a positive family history of SCD had a higher prevalence of diabetes mellitus, dyslipidemia, chronic coronary artery disease, and revascularization. These findings suggest that a family history of SCD may be helpful for identifying individuals who may benefit from earlier screening, risk stratification, and preventive measures.

Further research is needed to better understand the genetic and environmental factors contributing to SCD and to develop effective prevention strategies for this devastating condition.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## References

1. Adabag AS, Luepker RV, Roger VL, et al. Sudden cardiac death: epidemiology and risk factors *Nat Rev Cardiol.* 2010;7(4):216-25.
2. Zheng ZJ, Croft JB, Giles WH, et al. Sudden cardiac death in the united states, 1989 to 1998. *Circulation.*2001; 104(18):2158-2163.
3. Votýpka P, Krebsová A, Norambuena-Poustková P, et al. Post-mortem genetic testing in sudden cardiac death and genetic screening of relatives at risk: lessons learned from a Czech pilot multidisciplinary study. *Int J Legal Med.*2023;137(6):1787-1801.
4. Narayan SM, Wang PJ, Daubert JP. New concepts in sudden cardiac arrest to address an intractable epidemic: JACC state-of-the-art review. *J Am Coll Cardiol.* 2019;73(1):70-88.
5. Wong CX, Brown A, Lau DH, et al. Epidemiology of sudden cardiac death: global and regional perspectives. *Heart Lung Circ.*2019;28(1):6-14.
6. Davies M J. Anatomic features in victims of sudden coronary death. Coronary artery pathology. *Circulation.* 1992;85(1):119-24.
7. de Vreede-Swagemakers JJ, Gorgels AP, Dubois-Arbouw WI, et al. Out-of-hospital cardiac arrest in the 1990s: a population-based study in the Maastricht area on incidence, characteristics and survival. *J Am Coll Cardiol.*1997;30(6):1500-1505.
8. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics-2013 update: a report from the American Heart Association. *Circulation.* 2013;127(1):e6-e245.
9. Jouven X, Desnos M, Guerot C, et al. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation.*1999;99(15):1978-1983.
10. Ali AN, Abdeltawab HA, Eldamanhoury H, et al. Risk factors of sudden cardiac death in Egyptian patients younger than 40 years. *Egypt Heart J.*2023;75(1):45.
11. Khosravi A, Taylor R, Naghavi M, et al. Mortality in the islamic republic of Iran, 1964-2004. *Bull WHO.* 2007; 85(8):607-614.
12. Chugh SS, Jui J, Gunson K, et al. Current burden of sudden cardiac death: multiple source surveillance versus retrospective death certificate- based review in a large US community. *J Am Coll Cardiol.* 2004; 44(6):1268-75.
13. Hua W, Zhang LF, Wu YF, et al. Incidence of Sudden Cardiac Death in China: analysis of 4 regional populations. *J Am Coll Cardiol.* 2009;54(12):1110-8.
14. Tokashiki T, Muratani A, Kimura Y, et al. Sudden death in the general population in Okinawa: incidence and causes of death. *Jpn Circ J.*1999;63(1):37-42.
15. Patel M A, Malhotra A, Mpondo FHM, et al. Sudden cardiac death in the adolescent population: a narrative review. *Egypt J Intern Med.* 2023;35(1):36.
16. Dalgaard CV, Hansen BL, Jacobsen EM, et al. Sudden unexplained death versus nonautopsied possible sudden cardiac death: Findings in relatives. *J Cardiovasc Electrophysiol.* 2022; 33(2):254- 261.
17. Ferrero Miliani L, Holst AG, Pehrson S, et al. Strategy for clinical evaluation and screening of sudden cardiac death relatives. *Fundam Clin Pharmacol.* 2010;24(5): 619-635.
18. Myers RH, Kiely DK, Cupples LA, et al. Parental history is an independent risk factor for coronary artery disease: the Framingham Study. *Am Heart J.* 1990;120(4):963-969.
19. Podrid PJ. Overview of sudden cardiac arrest and sudden cardiac death. *UpToDate.* 2017; 1-50.
20. Spoon DB, Psaltis PJ, Singh M, et al. Trends in cause of death after percutaneous coronary intervention. *Circulation.* 2014;129(12):1286-94.
21. Friedlander Y, Siscovick DS, Weinmann S, et al. Family history as a risk factor for primary cardiac arrest. *Circulation.*1998; 97(2):155-160.
22. Milano A, Blom MT, Lodder EM, et al. Sudden cardiac arrest and rare genetic variants in the community. *Circ Cardiovasc Genet.* 2016; 9(2):147-53.
23. Chugh SS, Reinier K, Teodorescu C, et al. Epidemiology of sudden cardiac death: clinical and research implications. *Prog Cardiovasc Dis.* 2008;51(3):213-28.
24. Kaikkonen KS, Kortelainen ML, Linna E, et al. Family history and the risk of sudden cardiac death as a manifestation of an acute coronary event. *Circulation.* 2006;114(14):1462-1467.
25. Hamid L, Abdelfattah A, Hussien K, et al. Screening general population for family history of sudden cardiac death unmasks high risk individuals as potential victims (pilot study). *E J C CM.* 2018; 6(1):9-16.
26. Webster G, Olson R, Schoppen ZJ, et al. Cardiac Evaluation of Children With a Family History of Sudden Death. *J Am Coll Cardiol.* 2019;74(6):759-770.
27. Tan BY, Judge DP. A clinical approach to a family history of sudden death. *Circ Cardiovasc Genet.* 2012;5(6):697-705.
28. Tomaske M, Keller D I, Bauersfeld U. Sudden cardiac death: clinical evaluation of paediatric family members. *Europace.* 2011;13(3):421-426.
29. Rao MP, Al-Khatib SM, Pokorney SD, et al. Sudden Cardiac Death in Patients With Ischemic Heart Failure Undergoing Coronary Artery Bypass Grafting: Results From the STICH Randomized Clinical Trial (Surgical Treatment for Ischemic Heart Failure). *Circulation.*2017;135(12):1136-1144.