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Spectrum of Disorders Leading to Sudden Cardiac Death

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ABSTRACT

Objective: To determine the frequency of disorders leading to sudden cardiac death (SCD).
Study Design: Cross-sectional study.
Place and duration of study: Pathology Lab in collaboration with the Cardiology Department, AFIC & NIHD, Rawalpindi Pakistan, from Jan 2017 to Dec 2018.
Methodology: A total of 305 cases of sudden cardiac death reported within the last 24 hours of a death to AFIC Rawalpindi were included consecutively. Cases with a history of extracardiac diseases leading to sudden death were excluded. Most of the included cases were diagnosed phenotypically based on clinical examination, biochemistry, ECG, echocardiography, angiography, thallium scan, electro-physiological studies, cardiac CT scan, MRI and routine autopsy whenever recommended.
Results: Out of 305 cases, 197 (65%) were males and 108 (35%) females. Disorders leading to SCD were found in 178 (58.3%) cases due to ischemic heart disease (IHD), aortic dissection (0.7%), hypertrophic cardiomyopathy (HCM) (0.3%), dilated cardiomyopathy (DCM) (10.5%), congenital heart disease (12.1%) and valvular heart disease (7.9%). While in cardiac channelopathies, catecholaminergic polymorphic ventricular tachycardia (CPVT) in 5 (1.6%) and congenital long QT syndrome (LQTS) in 2 (0.7%) cases. However, 24 (7.9%) cases remained as sudden unexplained deaths (SUD).
Conclusion: In our setup, ischemic heart disease and dilated cardiomyopathy were the commonest causes of sudden cardiac death, followed by congenital heart disease and valvular heart diseases.

Keywords: Cardiac disorders, Ischemic heart disease, Sudden cardiac death.

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INTRODUCTION

Sudden cardiac death (SCD) is the unexpected death of an individual, not attributable to any extracardiac cause and usually occurs within 1 hour of symptoms onset (or in the last 24 hr, being seen in good health if death is unwitnessed). Sudden cardiac arrest (SCA) is the sudden, unexpected pulseless condition that usually arises from arrhythmias and can lead to SCD. Globally, almost more than 5 million people experience SCD annually, accounting for approximately 10-20% of the total mortality and 50% of cardiovascular mortality.[1] It is observed that almost 40% of SCA cases mostly reveal inherited cardiac disease on the genetic examination. Cases of sudden unexplained death (SUD) are approximately 15% of the total SCD.[2]

There are several causes of SCD, including structural heart diseases, e.g., ischemic heart disease (IHD) is mainly due to atherosclerotic cardiovascular disease (ASCVD). However, other forms of coronary artery disease (CAD), including thromboembolism, dissection and vasculitis, should also be kept in mind.[3] Structural causes due to non-ischemic cardiomyopathies leading to SCD include dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and restrictive cardiomyopathy (rare) and valvular heart disease.[4] At the same time, other rare structural causes of SCD include myocarditis, infiltrative cardiomyopathies (sarcoidosis, cardiac amyloidosis and cardiomyopathy associated with Fabry disease) and congenital heart diseases. In nonstructural causes, the most common cardiac channelopathies are catecholaminergic polymorphic ventricular tachycardia (CPVT), congenital long QT syndrome (LQTS)2, and Brugada syndrome (BrS) and rarely short QT syndrome (SQTS)[5].

Most cases of SCA are diagnosed phenotypically on the bases of clinical examination, biochemistry, electro-cardio-graphy (ECG), echocardiography (Echo), angiography, thallium scan, electro-physiological (EP) studies, magnetic resonance imaging (MRI), computerized cardiac tomography (CT) scan and routine autopsy if required.[6] In the last few years, there has been a significant increase in the knowledge about human genetics and the technologies based on studying the whole genome. A customized panel of

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cardiac gene analysis on next-generation sequencing (NGS) can help diagnose sudden unexplained deaths (SUD).[3,4,7]

The sadness suffered by families is aggravated by the risk of such deaths conferred upon the surviving relatives. For families of SCD victims, uncovering a definitive cause of death can help relieve the agonizing uncertainty and is a vital step in screening surviving relatives and instituting remedies to reduce SCA risk. The purpose of this study was to know the frequency of disorders leading to SCD that can further help in high-risk/family member implications for the disorders that can predispose the individuals for SCA.

METHODOLOGY

This cross-sectional study was conducted at the Pathology Lab in collaboration with the Cardiology Department, AFIC & NIHD, Rawalpindi Pakistan, from January 2017 to December 2018, after approval by the Institutional Ethical Review Board (Letter No.28/ 11/R&D/2019/39). Sample size calculated using WHO calculator, taking the prevalence of SCD 20% of total mortality,1 at 95 % confidence level and absolute precision of 0.05, sample size became 246. In addition, we included an additional 20% of cases for dropout (selected 305).

Inclusion Criteria: Cases of sudden cardiac death reported within the last 24 hours of death to AFIC Rawalpindi were included in the study.

Exclusion Criteria: Cases with a history of extracardiac diseases leading to sudden death were excluded from the study.

A total of 305 cases of sudden cardiac death were consecutively included after informed consent from attendants. Most cases were diagnosed phenotypically based on clinical examination, biochemistry, ECG2, Echo, angiography, thallium scan, EP studies, cardiac CT scan, MRI and routine autopsy whenever required for identifying causes of sudden cardiac death.[7,8]

Statistical Package for Social Sciences (SPSS) version 22.0 was used for the data analysis. Frequencies and percentages were calculated for qualitative variables like age groups, gender, HTN, DM and disorders causing SCD. In addition, mean and SD were calculated for quantitative variables, such as age.

RESULTS

Out of the 305 cases, 197 (65 %) were males and (108) 35% females, having a mean age of 55.0±22 years in males and 55.0±25 years in females. There were 38 (12.5%) patients in the less than five years age group, 3 (1.0%) in 5 to 25 years age group, 39 (12.8%) in the 26 to 45 years age group and 225 (73.3%) more than 45 years age group (Table).

Table: Baseline qualitative characteristics of the cases of sudden cardiac death (n = 305)

Parameters	n (%)
Age group-1, Age < 5 years	38 (12.5)
Age group-2, Age 5 – 25 years	3 (1.0)
Age group-3, Age 26 – 45 years	39 (12.8)
Age group-4, Age > 45 years	225 (73.8)
Males	197 (65.0)
Females	108 (35.0)
Hypertension	65 (21.3)
Diabetes Mellitus	52 (17.0)

Disorders leading to SCD were found in 178 (58.3%) cases due to ischemic heart disease (IHD), aortic dissection (0.7%), hypertrophic cardiomyopathy (HCM) (0.3%), dilated cardiomyopathy (DCM) (10.5%), congenital heart disease (12.1%) and valvular heart disease (7.9%). While in cardiac channelopathies, catecholaminergic polymorphic ventricular tachycardia (CPVT) in 5 (1.6%) and congenital long QT syndrome (LQTS) 2 (0.7%) cases. However, 24 (7.9%) cases remained as sudden unexplained deaths (SUD) (Figure).

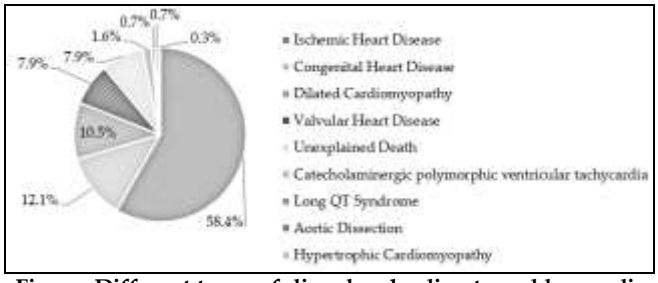

Figure: Different types of disorders leading to sudden cardiac death in total of 305 cases, reported to Armed Forces Institute of Cardiology Rawalpindi (n=305)

DISCUSSION

SCD is a major public health problem among the top contributors to the global burden of premature death. According to different studies in the literature, the relative prevalence of the causes of SCD, including structural heart diseases, e.g. ischemic heart disease (IHD), most commonly due to ASCVD, is 45 - 80%,[9] but other causes of CAD, including thromboembolism, dissection (0 – 2.3%) and vasculitis should also be kept in mind. Structural causes due to non-ischemic cardiomyopathies leading to SCD include HCM 8-35%, DCM 10-19%, restrictive cardiomyopathy (rare) and ARVC 12-28%, valvular heart disease 3-10 % and congenital heart diseases in 2–11%.[10,11] While other rare

structural causes of SCD include myocarditis and infiltrative cardiomyopathies (sarcoidosis, cardiac amyloidosis and cardiomyopathy associated with Fabry disease)[1]. In nonstructural causes, the most common cardiac channelopathies are LQTS 11-30%, Brugada syndrome 2 -12%, CPVT 9 - 37% and rarely SQTS.[12,13,14]

Isbister *et al.* in 2019 studied causes of SCD and identified CAD in 70%, cardiomyopathies in 15%, valvular heart disease in 5%, inherited arrhythmia syndromes in 2% and other causes of SCD in 8% cases.[1] Our study showed a bimodal distribution of age with an initial peak at less than five years of age and a much larger peak in the old age group, similar to other studies in literature.[15] SCD is found more common in males than in females. The leading cause of SCD is IHD.[9] Structural causes of SCD can be easily diagnosed phenotypically on available investigations and routine autopsy findings; that is why the percentage of IHD, DCM, congenital heart diseases, and valvular heart diseases is more in our study. On the other hand, nonstructural causes of SCD or channelopathies can only be diagnosed when electrical activity is there for ECG and EP studies before death.[16] That is why the percentage of LQTS and CPVT was less in our study, as genetic testing was not done.

It may be proposed that channelopathies (LQTS, BrS and CPVT) can be more common in SUD, which can further be diagnosed correctly by a cardiac panel of customized genes testing on NGS,[16] or by analyzing on multiplex DNA q-PCR.[17] Genetic testing is the only solution to diagnose unexplained death.[3] SUD are those deaths where the cause could not be found after detailed premorbid history and a complete routine autopsy. In these cases, analysis of the heart by an expert cardiac pathologist and genetic testing is recommended.[18] Many familial conditions are inherited in an autosomal dominant fashion such that 50% of the first-degree relatives have gene mutation.[1,19] Therefore, investigating the cause of death in cases of SCD is vital in caring for the surviving relatives. That can help to prevent further SCA events.[3]

LIMITATIONS OF STUDY

The limitation of the study was that this was a cross-sectional study, and genetic testing was not performed in a sudden unexplained death.

Hence, it is proposed that future studies should be carried out to perform target sequencing on NGS to diagnose genetic disorders leading to SCD. Furthermore, an autopsy was not carried out in all cases; rather, it was only performed in a few recommended cases and where permission was given to perform an autopsy. Therefore, further studies are required where molecular autopsy may be performed.

CONCLUSION

In our setup, ischemic heart disease and dilated cardiomyopathy were the commonest causes of SCD, followed by congenital heart disease and valvular heart diseases. The causes of SCA differ in various regions, and the management of SCA depends on the cause. So knowing the frequency of most common causes of sudden cardiac death in our setup could be helpful in the early diagnosis of the disease and further management of an affected patient. This can positively impact the lives of first-degree relatives of the victims of SCD, who can get preventive therapies by early diagnosis.

Conflict of interest: None.

Author's Contribution

STAG: Pathological investigation, interpretation of data, responsibility for the manuscript, DAK: Biostatistics, GI: Paper writing, KAK: Case selection, interpretation of investigations, AR: Case selection, AHS: Responsibilty for the manuscript and paper writing.

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