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PATTERNS AND PATHOLOGICAL CAUSES OF SUDDEN DEATH IDENTIFIED THROUGH AUTOPSY

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Abstract
Objective: To determine the histopathological patterns and underlying causes of sudden death (SD) through autopsy.
Study Design: A retrospective case series.
Place and Duration: This study was conducted at, Jinnah Sindh Medical University (JSMU) Karachi January 2022 to January 2025.
Methods: This study analyzed 45 cases of SD selected from a total of 100 medico-legal autopsies. Cases involving trauma, suicide, or homicide were excluded. Standard gross and microscopic examinations were performed, and histopathological findings were reviewed. Statistical analysis was carried out using SPSS v21.0, with results expressed as frequencies, percentages, and means with standard deviations.
Results: The age of the deceased ranged from 24 to 47 years (mean ± SD: 35.7 ± 3.3 years). The highest frequency was observed in the 36–40-year group (n = 15, 33.3%), followed by 31–35 years (n = 12, 26.7%). Cardiovascular causes were identified in 25 cases (55.6%), with coronary artery disease (CAD) being the leading pathology (n = 15, 60.0%). Other cardiac causes included myocarditis (n = 2, 8.0%), cardiomyopathies (n = 2, 8.0%), and coarctation of the aorta (n = 1, 4.0%). Non-cardiac causes accounted for 20 cases (44.4%), with pulmonary causes (n = 5, 25.0%), septicemia (n = 3, 15.0%), and cerebrovascular events (n = 3, 15.0%) being most common.
Conclusion: Cardiovascular pathology, particularly CAD, is the predominant cause of sudden death in this cohort. Integration of molecular autopsy in unexplained cases and improved public health strategies targeting early risk detection are recommended.

Keywords: Sudden death, Autopsy, Coronary artery disease, Cardiovascular pathology, Histopathology

Introduction

Sudden death (SD) is defined as an unexpected fatal event occurring within 24 hours of symptom onset [1]. It represents a significant global public health concern, with sudden cardiac death (SCD) accounting for approximately 6-20% of all deaths worldwide [2]. SCD is characterized by an unexpected death due to cardiac causes, occurring within a short period (generally within an hour of symptom onset) in a person with known or unknown cardiac disease [3]. SD is most commonly caused by cardiovascular diseases. The most frequently observed of these diseases is coronary artery disease (CAD). Other significant cardiac causes include dilated cardiomyopathy, accounting for 43.9% of cases, and cardiac hypertrophy, observed in 36.07% of cases [4]. Inflammation of the heart muscle, known as myocarditis, can also lead to sudden death. It accounts for around 20% of such deaths in young adults [5]. Prominent among non-cardiac causes are pulmonary embolism and cerebral hemorrhage [2]. In several populations, respiratory conditions, including pneumonia, are believed to account for 18.7% of sudden deaths [6]. It is crucial to identify at-risk individuals quickly. Routine check-ups for cardiovascular risk, genetic testing for some inherited heart problems, and implantable cardioverter-defibrillators (ICDs) in at-risk individuals help reduce the risk of SCD [7].

After an individual passes away, an autopsy or post-mortem examination is performed to reveal the cause, manner and the circumstances of death [8]. There are two main types of autopsies: clinical (or hospital) and medico-legal (or forensic). When the family agrees, a clinical autopsy is carried out to learn more about diseases, evaluate various treatments or for educational purposes. Meanwhile, medico-legal autopsies are needed by the law when a death is sudden, not explained by any means or looks suspicious to help in the investigation [9]. Nowadays, molecular autopsies are taking the place of standard autopsies. Molecular autopsies, when using post-mortem genetic tests, can discover the pathogenic mutations behind arrhythmogenic syndromes and, as a result, reveal new causes of death that may be missed by traditional autopsies [10].

Since the mid-20th century, the number of autopsies being conducted worldwide has declined. The proportion of autopsies in the United States has decreased, from being carried out approximately half the time in the 1960s to fewer than 5% today [11]. A similar trend has also been observed worldwide, including in the United Kingdom and Germany [11]. In many developing countries, it is more challenging to perform autopsies. Often, religious and cultural customs stop people from allowing post-mortem examinations. In addition, a shortage of resources, poor infrastructure and fewer trained individuals prevent many areas from providing autopsy services [12].

In Pakistan, data about the causes of sudden death among young adults is scarce. In Jhelum, researchers studied 34 autopsies that were performed on men in the government who died suddenly. In 41.2% of the cases, death was due to coronary atherosclerosis [13]. As a result, localized studies are needed to understand SD epidemiology better and design appropriate strategies to prevent cases. This study aims to fill this gap by studying the causes of sudden death, using autopsy data on 45 cases admitted to a tertiary care hospital. Determining the frequency of cardiac and non-cardiac causes of SD and investigating the histopathological patterns among the cases are the primary objectives of this study.

Methodology

This retrospective case series was initiated following formal approval from the Institutional Ethical Review Board. Written informed consent was obtained from the legal attendants of the deceased individuals included in the study.

The research focused exclusively on sudden deaths, defined as fatalities occurring within 24 hours of the onset of clinical symptoms. All age groups were considered eligible for inclusion, ensuring a comprehensive demographic representation. However, cases involving unnatural causes of death, such as those resulting from road traffic accidents, suicide, homicide, or blast injuries, were systematically excluded to preserve the clinical and pathological integrity of the study.

Data was retrospectively retrieved from hospital admission records, autopsy registers, and postmortem reports maintained at hospital. Information such as duration of hospital stay prior to death, clinical assessments, and preliminary cause of death provided by attending physicians was documented. All autopsies were performed in accordance with standard medico-legal procedures in the hospital's designated autopsy suite. Initial external examinations included assessments of postmortem interval indicators such as lividity, rigor mortis, and visible external abnormalities or trauma.

Comprehensive internal examinations were then carried out, targeting signs of pathological processes including pneumothorax, hemothorax, pericardial effusion, gastrointestinal perforation, intra-abdominal fluid accumulation, and vascular anomalies such as coarctation of the aorta and aneurysms. Major organs from various systems were dissected and collected for both gross inspection and detailed histomorphological evaluation. Tissues were preserved in 10% buffered formalin, processed, and sectioned at 4-5 mm thickness. These sections were subsequently embedded in paraffin, cut into 4 µm slices using a rotary microtome, and stained with hematoxylin and eosin (H&E) for microscopic evaluation.

In cases where the cause of death remained unclear or where poisoning was suspected, viscera samples, including stomach, small intestine, liver, and kidneys, were collected for toxicological analysis. These specimens were forwarded to the Punjab Forensic Science Agency (PFSA) in Lahore for comprehensive chemical examination to rule out any toxicological involvement.

All collected data were compiled and analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0. Quantitative variables were expressed as means with standard deviations (Mean ± SD), while categorical variables were presented as frequencies and percentages to facilitate descriptive statistical interpretation.

Results

During the period of study , a total of 100 autopsies were conducted. Out of these, 45 cases met the criteria for sudden death and were included in the study. The age of the deceased ranged from 24 to 47 years, with a mean age of 35.7 ± 3.3 years. The highest frequency of sudden death was observed among individuals aged 36 to 40 years, followed by the 31 to 35 age group. **Table 1** presents the distribution of cases across age groups. The majority of deaths occurred in the 36-40 age bracket (33.3%), while the lowest frequency was recorded in individuals aged 46-50 years (6.6%).

Table 1: Age Distribution of Sudden Deaths (n=45)

Age Range (years)	Frequency (n)	Percentage (%)
20 to 30	8	17.8%
31 to 35	12	26.7%
36 to 40	15	33.3%
41 to 45	7	15.6%
46 to 50	3	6.6%

Histopathological findings indicated that 25 out of 45 deaths (55.6%) were due to cardiovascular causes. Among these, coronary artery disease emerged as the predominant pathology, found in 15 cases (60.0%). Other cardiovascular causes included cardiomyopathies and myocarditis, accounting for 2 cases each (8.0%), while coarctation of the aorta was observed in 1 case (4.0%). In 5 cases (20.0%), the exact cardiac cause remained unascertained despite detailed examination.

Table 2: Cardiac Causes of Sudden Deaths (n = 25)

Disease	n (%)	Percentage (%)
Coronary artery disease	15	(60.0%)
Cardiomyopathies	2	(8.0%)
Myocarditis	2	(8.0%)
Coarctation of aorta	1	(4.0%)
Unascertained	5	(20.0%)

The remaining 20 cases (44.4%) were attributed to non-cardiac causes. Pulmonary causes, such as pneumonia and embolism, accounted for the highest proportion among these (n = 5, 25.0%). Both septicemia and cerebrovascular events were identified in 3 cases each (15.0%). Enteric perforation was observed in 2 cases (10.0%), and multi-organ failure (renal and hepatic) accounted for 1 case (5.0%). The "others" category, including less frequent etiologies such as metabolic or endocrine causes, comprised 6 cases (30.0%).

Table 3: Non-Cardiac Causes of Sudden Deaths (n = 20)

Disease	n (%)	Percentage (%)
Pulmonary causes	5	(25.0%)
Septicemia	3	(15.0%)
Cerebrovascular causes	3	(15.0%)
Enteric perforation	2	(10.0%)
Renal and liver failure	1	(5.0%)
Others	6	(30.0%)

Discussion

The present study aimed to investigate the histopathological causes of SD among 45 cases undergoing autopsy. In our study, the highest frequency of sudden death cases was observed in the 36-40-year age group (33.3%), followed by the 31-35-year group (26.7%). This distribution is consistent with a Danish nationwide study, which found that the annual incidence rate of SCD increased from 2.3 per 100,000 persons in the 1-35 age group to 21.7 per 100,000 in the 36–49 age group [14]. Another U.S. study by Richard et al. found that persons aged 31 to 35 years had the highest incidence of SCD, at 3.2 cases per 100,000 persons per year [15].

According to this study, 55.6% of the sudden deaths were found to be caused by cardiovascular issues, and CAD was the most common, making up 60% of them. These observations come from worldwide data, proving that CAD is commonly a primary reason for SCD. As reported by Singh et al. (2023) in their study, atherosclerosis and myocardial infarction were the most frequent findings at autopsy, seen in 70.2% and 45.6% of cases [16]. A Romanian investigation discovered that approximately 89.8% of all cases of sudden death were caused by coronary atherosclerotic disease [4]. Sudden cardiac death in younger people is primarily due to myocarditis. This corresponds with a study by Lynge et al. (2019) from Denmark that noted that 6% of SCD autopsies were due to myocarditis, and percentages were higher in younger people [17].

Histopathology tests were unable to clarify the reason for almost one in five deaths in this investigation. Substantial research reveals that 30% of sudden heart deaths cannot be easily explained by typical autopsies [18]. This phenomenon is known as "autopsy-negative sudden death," and that makes it difficult for forensic pathologists [10]. Molecular autopsy helps reveal many diseases, including inherited arrhythmia disorders after a person has died [18]. Using molecular autopsy, scientists can now find genetic differences associated with sudden-death syndromes, such as long QT syndrome and Brugada syndrome [18]. According to a systematic review, molecular autopsies might explain the cause of death for one of every five cases where the reason was unknown [19].

Sudden death in this study was most likely to occur due to a non-cardiac reason (44.4%). Pneumonia and embolism represented 25% of the non-cardiac deaths. A systematic review also made a similar observation that sudden non-cardiac deaths are likely to be due to respiratory diseases and disseminated diseases [20]. Death in 15% of cases within this study was due to septicemia and cerebrovascular events. These results are in line with research that has found sudden death as a result of infection and cerebrovascular events. Additionally, another study of young adult deaths found that most sudden deaths were caused by nonheart problems such as infections and cerebrovascular events [21].

This study is limited by its small sample size (45 sudden death cases), which may limit the generalizability of these results to other larger-scale populations. Additionally, as a single-center retrospective study, there are potential biases in case selection and data recording. Furthermore, the

unavailability of advanced diagnostic tools, such as molecular autopsy in unascertained cases, limits the identification of genetic or inherited arrhythmogenic causes.

Conclusion
The finding of this study suggests that most sudden deaths in young to middle-aged people are due to cardiovascular causes, chiefly coronary heart disease. These results underscore the importance of early screening, public health education and lifestyle interventions for modifiable risk factors. Incorporation of molecular autopsy into cases of unexplained death greatly enhances diagnostic accuracy and family risk assessment. Strengthening the infrastructure for autopsy and adding advanced diagnostics will go a long way toward improving our understanding and preventing sudden unexplained deaths.

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