

Histomorphological Spectrum of Various Systems in Sudden Deaths: An Autopsy Study at a Tertiary Care Centre in Gujarat, India

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ABSTRACT

Introduction: The phenomenon of sudden death is a concern, despite tremendous technological advances in healthcare. Sudden death in adults without any past history of chronic illness is increasing worldwide and is a significant issue for medical professionals. In this modernised medical world, diagnostic tools lack precision in comparison to autopsy cause of death when it comes to finding the clinical cause of death. The World Health Organisation (WHO) defines sudden death, according to the International Classification of Diseases, version 10 (ICD-10), as non violent death occurring less than 24 hours from the onset of symptoms, without any other explanation.

Aim: To examine the different histomorphological changes observed in autopsy specimens of sudden deaths.

Materials and Methods: This retrospective descriptive cross-sectional study was conducted in the Department of Pathology at a Tertiary Care Hospital affiliated with a Medical College in South Gujarat, India. Data was collected from autopsies performed between January 2018 and December 2019, and the study was conducted from January 2020 to December 2021. A total of 430 cases of sudden death were systematically examined during the study period. The autopsy forms were used to retrieve the history, and all slides from the 430 cases were reviewed. The history, gross findings, and microscopic features were noted and entered into an Excel sheet.

Results: A total of 1671 autopsies were performed during the study period, out of which 430 were sudden deaths. The most commonly affected age group was 41-50 years, with 114 cases (26.51%), followed by the 31-40 years age group with 101 cases (20.16%). Among the cases, 387 were males and 43 were females, resulting in a male-to-female ratio of 9:1. The most common cause of sudden death was cardiovascular pathology 267 (62.10%). Non cardiac causes were attributed to respiratory system involvement 79 (18.37%), followed by cases where no specific cause was identified 43 (10%), multiple system involvement 28 cases (6.51%), hepatobiliary causes 7 (1.62%), genitourinary system causes 4 (0.94%), and Central Nervous System (CNS) causes 2 (0.46%).

Conclusion: The present study revealed a significant number of cases of sudden natural death. Cardiac causes were found to be the major contributor to sudden death, posing a health concern in our society. Atherosclerosis was identified as the main culprit in causing myocardial infarction. Sudden death remains a significant concern, and a meticulous postmortem and histopathological {Haematoxylin & Eosin (H&E)} examination are necessary to determine its cause. To prevent sudden natural deaths, it is essential to educate the population about the importance of undergoing annual health check-ups for early diagnosis and treatment.

Keywords: Cardiovascular causes, Natural death, Non cardiac causes

INTRODUCTION

The phenomenon of sudden death remains a concern despite significant technological advancements in healthcare. Sudden death in adults without a history of chronic illness is increasing globally and is a matter of concern for medical professionals. Even in this modernised medical world, diagnostic tools lack precision in determining the clinical cause of death compared to autopsy findings. The primary objective of an autopsy is to determine the most probable cause of death. According to the WHO definition in the ICD-10, sudden death refers to non violent deaths that are unexplained and occur within 24 hours from the onset of symptoms [1]. Sudden deaths are more common in males than females [2,3]. Due to the nature of sudden death, an accurate diagnosis is challenging to achieve without an autopsy [1]. Risk factors for sudden death include older age, low and high body mass index, arterial hypertension, diabetes mellitus, smoking, sedentary lifestyle, unhealthy diet, and stress [4]. Sudden death accounts for approximately 10 percent of all deaths. Cardiovascular causes such as coronary artery disease, myocardial infarctions, cardiomyopathies, aortic dissection, aneurysms, and myocarditis are commonly associated with sudden death. Studying sudden death helps identify the causes of death and can assist legal authorities in detecting crimes and providing solace to grieving relatives when medical negligence is suspected.

Numerous studies have been conducted on this topic in the past, but due to changing lifestyles, sudden deaths are increasing in young adults. Therefore, periodic studies are necessary to understand the recent trends in gender and age distribution, as well as the causes of sudden death cases, in order to prevent these unexpected deaths. The purpose of the present study was to identify different causes of sudden death, observe morphological changes in various organs after death, and provide new insights into the study of sudden death, which will aid in patient care and the prevention of premature deaths.

MATERIALS AND METHODS

The present retrospective descriptive cross-sectional study was conducted in the Department of Pathology at a Tertiary care Hospital affiliated with Medical College in Surat, Gujarat, India. The study was conducted from January 2018 to December 2019. Ethical clearance for the study was obtained from the Human Research Ethics Committee of the Medical College and the Hospital where the study was conducted (IEC number: GMCS/STU/ETHICS/Approval/10608/20 - Protocol no: 113/20).

Inclusion and Exclusion criteria: Non traumatic, natural deaths occurring within 24 hours of the onset of acute signs or symptoms in an apparently healthy individuals, with or without previously diagnosed fatal conditions. Deaths occurring outside the hospital, in

the casualty, or as "dead on arrival". The cases included in the study were all the specimens received in the Department of Pathology, excluding autolyzed specimens.

Case of sudden death were systematically examined during the study period. The autopsy form was used to retrieve the history. Clinically relevant findings and gross findings were noted. All the slides were reviewed, and histopathological findings were recorded. Blocks of the same were retrieved, when required.

STATISTICAL ANALYSIS

Patient details, along with gross and histomorphological findings, were entered into an Excel sheet. Descriptive statistical analysis was performed, appropriate charts and graphs were created, and the results were expressed as a percentage.

RESULTS

A total of 1,671 autopsies were received, out of which 430 were sudden deaths, accounting for 25.73% of all autopsies. The age of the patients ranged from two days to 87 years. The highest number of cases (114 cases) was observed in the 41-50 years age group, representing 26.51% of the total. The 31-40 age group had 101 instances (20.16%). There were 91 cases (21.16%) in the 51-60 years age group, 50 cases (11.62%) in the 21-30 years age group, 42 cases (9.76%) in the 61-70 years age group, and 16 cases in the 71-80 years age group. Among those aged 0-10 years, there were four cases (0.93%). Strikingly, 387 (90%) of the cases were males, and only 43 (10%) were females, indicating a male predominance with a ratio of 9:1 [Table/Fig-1].

Age (Years)	Total	Percentage	Male	Percentage	Female	Percentage
0-10	4	0.93%	0	0%	4	9.30%
11-20	10	2.32%	9	2.32%	1	2.32%
21-30	50	11.62%	44	11.36%	6	13.95%
31-40	101	23.48%	92	23.77%	9	20.93%
41-50	114	26.51%	109	28.16%	5	11.62%
51-60	91	21.16%	86	22.22%	5	11.62%
61-70	42	9.76%	32	8.26%	10	23.25%
71-80	16	3.72%	14	3.61%	2	4.65%
81-90	2	0.46%	1	0.25%	1	2.32%
Total	430		387		43	

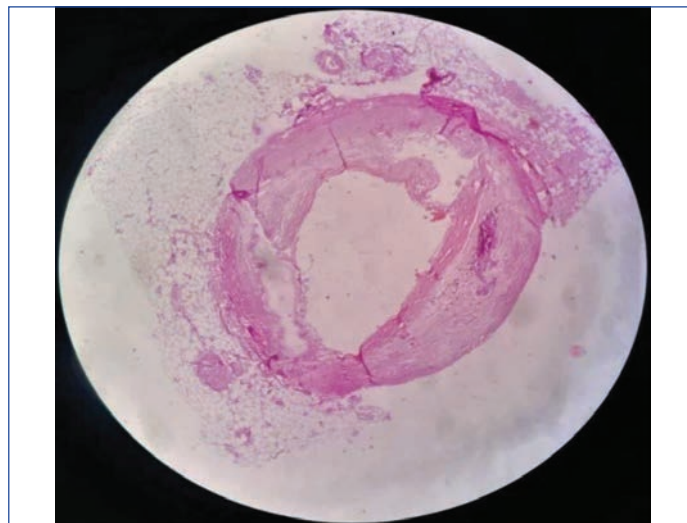
[Table/Fig-1]: Age and gender-wise distribution of sudden death cases (N=430).

Out of the total 430 sudden death cases, the cause of death was attributed to the cardiovascular system in 267 cases, accounting for 62.10%. The respiratory system was the cause in 79 cases (18.37%), and multiple system involvement was observed in 28 cases (6.51%). In 43 cases (10% of the total sudden death cases), no specific cause of death was found. Hepatobiliary causes accounted for 7 cases (1.62%), while genitourinary system involvement was observed in 4 cases (0.94%), and central nervous system involvement in 2 cases (0.46%) [Table/Fig-2].

Cause of death	Cases	Percentages
Cardiovascular system	267	62.10%
Respiratory system	79	18.37%
Other systems	41	9.53%
Hepatobiliary system	7	1.62%
Genitourinary system	4	0.94%
Central nervous system	2	0.46%
Multiple system involvement	28	6.51%
No specific cause identified	43	10%
Total	430	100%

[Table/Fig-2]: System-wise distribution of sudden death cases (N=430).

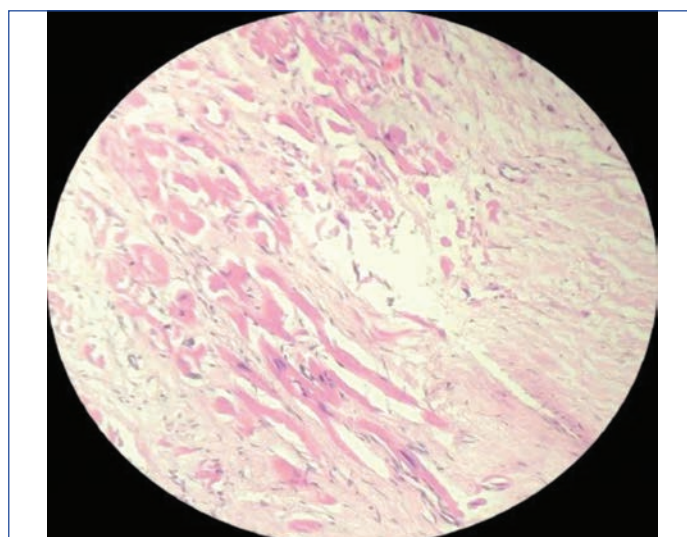
Among the 267 cases related to the cardiovascular system, the major cause identified was atherosclerosis alone [Table/Fig-3] (125 cases), followed by healed/old myocardial infarction with atherosclerosis [Table/Fig-4,5] (87 cases). Myocarditis alone [Table/Fig-6] was found in four cases (1.50%), while myocarditis with atherosclerosis was observed in three cases (1.12%). Additionally, two cases of aortic dissection were identified [Table/Fig-7].



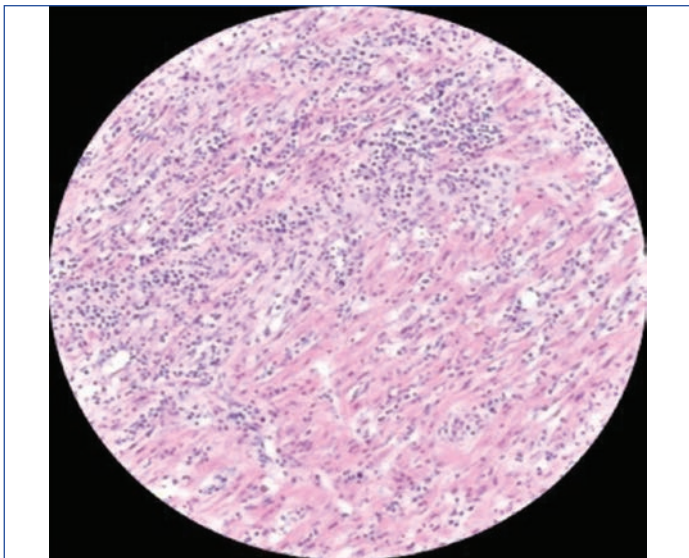
[Table/Fig-3]: Fibro Calcific Plaque plaque composed of lipid accumulation along with calcification (H&E, 4x).



[Table/Fig-4]: Gross image of healed myocardial infarction whitish well-demarcated fibrous scar at the apex of heart.



[Table/Fig-5]: Healed Myocardial Infarction scar tissue composed of collagen deposition without cellular infiltration (H&E, 40x).



[Table/Fig-6]: Myocarditis dense lymphohistiocytic infiltration within myocardial fibres without myocyte necrosis (H&E, 10X).

Cardiovascular system	Cases	Percentage
Atherosclerosis only	125	46.82%
Acute/Recent myocardial infarction with atherosclerosis	40	14.98%
Healed/Old myocardial infarction with atherosclerosis	87	32.58%
Recent and healed myocardial infarction with atherosclerosis	6	2.25%
Myocarditis	4	1.50%
Myocarditis with atherosclerosis	3	1.12%
Aortic dissection	2	0.75%
Total	267	100%

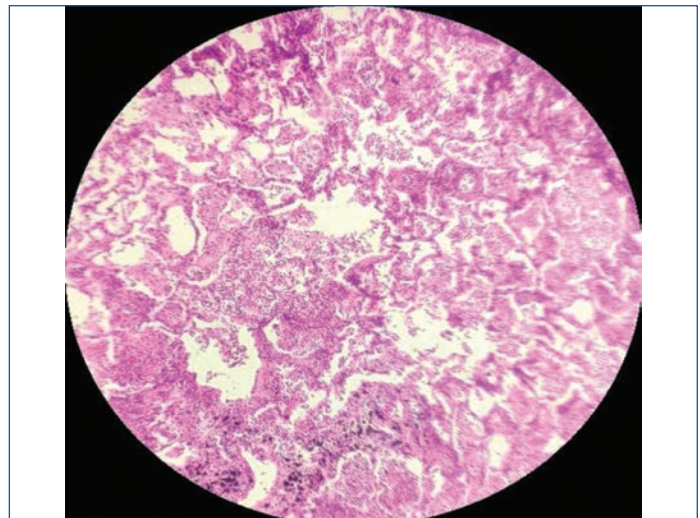
[Table/Fig-7]: Histopathological spectrum in cardiovascular system in sudden death cases (n=267).

Respiratory system involvement was seen in 79 cases (18.37%), including 29 cases of pneumonia [Table/Fig-8,9] (36.71%), 24 cases (30.38%) of pulmonary oedema, 3 cases of pulmonary haemorrhage (3.79%), 11 cases of tuberculosis [Table/Fig-10] (13.92%), 2 cases of pneumonia with tuberculosis (2.53%), 8 cases of pulmonary oedema with pulmonary haemorrhage (10.13%), one case of atelectasis with pneumonia, and one case of adenocarcinoma [Table/Fig-11].

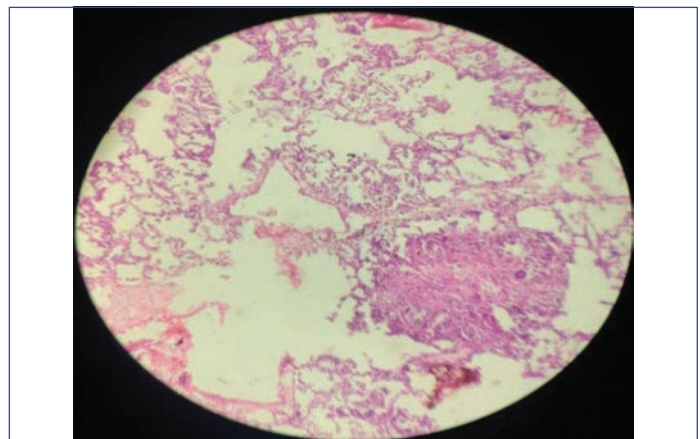


[Table/Fig-8]: Gross image of Pneumonia reddish congested lesion in part of one lobe of lung.

Among other systems, hepatobiliary system involvement (1.62%) includes six cases of cirrhosis [Table/Fig-12] and one case of a liver abscess. Genitourinary system involvement (0.94%) consists of one case of chronic glomerulonephritis, two cases of chronic pyelonephritis, and one case of acute tubular necrosis. Central nervous system involvement (0.46%) includes 1 case of subarachnoid



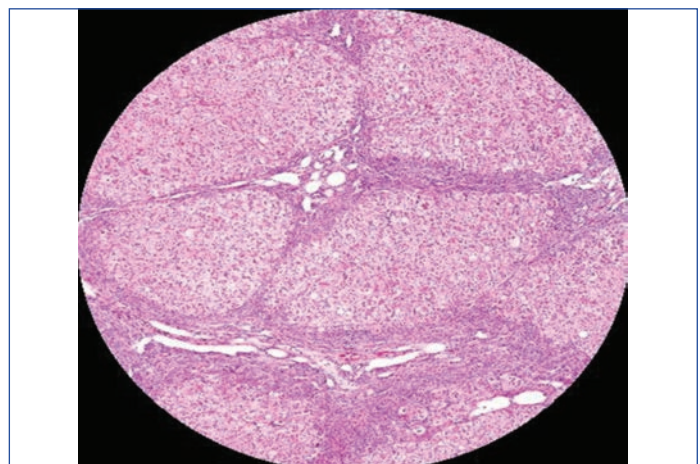
[Table/Fig-9]: Pneumonia alveoli of lungs filled with neutrophils (H&E, 10x).



[Table/Fig-10]: Tuberculosis of lung caseating granuloma in lung parenchyma (H&E, 10x).

Respiratory system	Cases	Percentage
Pneumonia	29	36.71%
Pulmonary oedema	24	30.38%
Pulmonary haemorrhage	3	3.79%
Tuberculosis	11	13.92%
Adenocarcinoma	1	1.26%
Pneumonia with tuberculosis	2	2.53%
Pulmonary oedema with pulmonary haemorrhage	8	10.13%
Atelectasis with pneumonia	1	1.26%
Total	79	100%

[Table/Fig-11]: Histopathological spectrum in respiratory system in sudden death cases (n=79).



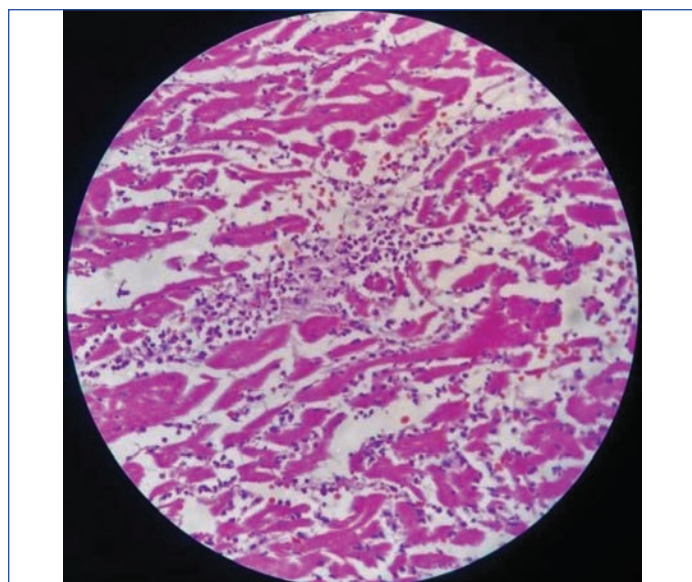
[Table/Fig-12]: Cirrhosis of Liver hepatocytes arranged in nodules separated by fibrous septa (H&E, 40x).

haemorrhage and one case of pyogenic meningitis. There were 28 cases (6.51%) showing involvement in more than one system, including diffuse alveolar damage with acute tubular necrosis in one case, disseminated tuberculosis in two cases, ischaemic heart disease with pneumonia in five cases, and ischaemic heart disease with pulmonary haemorrhage in five cases. Ischaemic heart disease with cirrhosis was found in three cases of sudden death. There were a total of 12 cases in which sickle cell disease was found. Among them, two cases also had cirrhosis along with sickle cell disease. Ischaemic heart disease with sickle cell disease was found in nine cases. In one case of sickle cell disease, subdural haemorrhage with ischaemic heart disease was identified [Table/Fig-13].

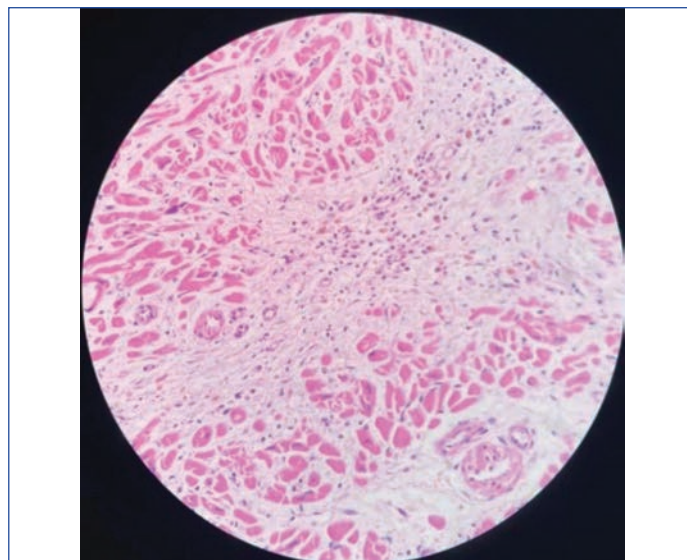
Cause of death	Cases
Hepatobiliary system	7
Cirrhosis	6
Liver abscess	1
Genitourinary system	4
Chronic glomerulonephritis	1
Chronic pyelonephritis	2
Acute tubular necrosis	1
Central nervous system	2
Subarachnoid haemorrhage	1
Pyogenic meningitis	1
Multiple system involvement	28
Diffuse alveolar damage+Acute tubular necrosis	1
Disseminated tuberculosis	2
Ischaemic heart disease with pneumonia	5
Ischaemic heart disease with pulmonary haemorrhage	5
Ischaemic heart disease with cirrhosis	3
Sickle cell disease with other systems involvement	12
Total	41

[Table/Fig-13]: Histopathological spectrum in other system in sudden death cases (n=41).

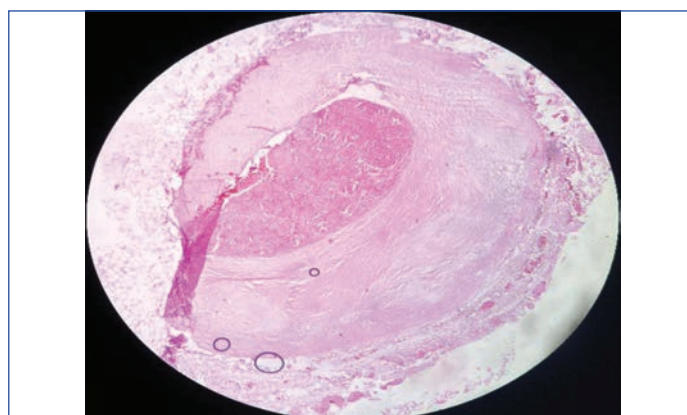
Out of 267 cases of cardiovascular system involvement, the major cause found was atherosclerosis only (125 cases), followed by healed/old myocardial infarction with atherosclerosis (87 cases), acute/recent myocardial infarction [Table/Fig-14,15] with atherosclerosis (40 cases), and six cases of both recent and healed myocardial infarction with atherosclerosis. Therefore, myocardial infarction was seen in a total of 133 cases (87+40+6). There was also a single case of antemortem thrombus in the coronary artery [Table/Fig-16].



[Table/Fig-14]: Acute Myocardial Infarction (AMI) dense polymorphonuclear neutrophilic infiltration along with coagulative necrosis (H&E, 40x).



[Table/Fig-15]: Healing Myocardial Infarction granulation tissue consists of loose collagen, pigment laden macrophages and capillary (H&E, 40x).



[Table/Fig-16]: Ante mortem Thrombus of coronary artery near total obstruction of the lumen of coronary artery by thrombus (H&E, 4x).

There were a total of 43 cases in which no specific cause of death was identified. Since authors received limited organs such as the heart, lung, liver, spleen, kidney, and brain, other causes of sudden death like gastrointestinal or pancreatic causes could not be identified in cases of sudden death.

DISCUSSION

In the present study, out of a total of 1671 received autopsies, 430 (25.73%) were sudden death cases. The Azmak AD study reported a consistent percentage of 28.98% (278/959) [5]. However, Sane M et al., found a lower percentage of 9% (159/1767) [6]. The most common age group (26.51%) in the present study was 41-50 years, which is consistent with the findings of Sane M et al., (41-50 years) and Joshi C (41-60 years). In contrast, Pandian JR et al., reported the most common age group as 31-35 years [Table/Fig-17] [5-8].

Author's name, Place/year of study	Most common age group	Percentages
Azmak AD [5] (N=278) (Turkey) (2006)	50-59 years	21.58%
Sane M et al., [6] (N=159) (Aurangabad, India) (2013)	41-50 years	30.81%
Pandian JR et al., [7] (N=120) (Manipur, India) (2014)	31-35 years	18.33%
Joshi C [8] (N=115) (Raipur, Chhattisgarh) (2016)	41-60 years	58.26%
Present study (N=430)	41-50 years	26.51%

[Table/Fig-17]: Comparative analysis of age-wise distribution of sudden death cases [5-8].

The maximum number of sudden death cases in the present study were attributed to the cardiovascular system (62.10%), followed by the respiratory system (18.37%). These findings are comparable to the studies conducted by Nofal HK et al., Narsireddy R et al.,

Chaudhari V and Mohite S Pandian JR et al., and Rastogi P et al., which also reported similar results [1-3,7,9]. However, Khan DF found that the most common causes of sudden death were related to the cardiovascular system, followed by the renal system [Table/Fig-18] [1-3,5-7,9,10].

Author's name, Place/year of study	Most common system involved	2 nd most common system involved
Sane M et al., [6] (N=159) (Aurangabad, India) (2013)	CVS (44.6%)	Respiratory system (25.78%)
Nofal HK et al., [1] (N=223) (Saudi Arabia) (2011)	CVS (59.2%)	Respiratory system (24.7%)
Azma AD [5] (N=278) (Turkey) (2006)	CVS (55%)	Respiratory system (19.1%)
Pandian JR et al., [7] (N=120) (Manipur, India) (2014)	CVS (55.83%)	Respiratory system (16.67%)
Narsireddy R et al., [2] (N=60) (Andhra Pradesh, India) (2020)	CVS (63.3%)	Respiratory system (23.3%)
Rastogi P et al., [9] (N=274) (Mangalore, India) (2011)	CVS (45%)	Respiratory system (25%)
Chaudhari V and Mohite S [3] (N=230) (Pondichery, India) (2012)	CVS (75.22%)	Respiratory system (15.65%)
Khan DF [10] (N=108) (Bangladesh) (2019)	CVS (42.59%)	Renal system (30.36%)
Present study (N=430)	CVS (62.10%)	Respiratory system (18.37%)

[Table/Fig-18]: Comparison of histopathological spectrum of causes of sudden death cases [1-3,5-7,9,10].

Atherosclerosis was identified as the major cause of sudden cardiac death (97.75%), which is consistent with the findings of Agale SV et al., (2018) in Mumbai, India [11] and Sonawane SY et al., (2017) in Solapur, Maharashtra [12], who reported percentages of 35.98% and 72.58% for sudden cardiac deaths, respectively. The second most common cause was myocardial infarction (49.81%), which is consistent with the studies conducted by Chaudhari V and Mohite S Rao D et al., and Sonawane SY et al., [3,12,13]. In the present study, all cases of myocardial infarction were associated with coronary atherosclerosis, which is also reported in the studies by Sonawane SY et al., and Escoffery CT and Shirley SE [13,14].

Regarding sudden death cases involving the respiratory system, the majority were due to pneumonia (36.71%), which is comparable to the findings of Narsireddy R et al., Chaudhari V and Mohite S and Azma AD, who reported percentages of 64.29%, 86.11%, and 84.90% for respiratory causes due to pneumonia, respectively [2,3,5]. The second most common cause of death within the respiratory system in the present study was pulmonary oedema (30.38%), which differs from the findings of other studies.

Among hepatobiliary causes, cirrhosis was found in six cases, and a liver abscess was found in one case as the main causes of sudden death. In contrast, Sane M et al., reported thr 3 cases (1.88%) of death due to cirrhosis and no cases of liver abscess [6].

There were only four sudden death cases with exclusive involvement of the genitourinary system. Among them, chronic glomerulonephritis was observed in one case, chronic pyelonephritis in two cases, and acute tubular necrosis in one case. In Sane M et al., study, pyonephrosis was found in only three cases among genitourinary causes [Table/Fig-19] [1,6,10].

Central nervous system causes included subarachnoid haemorrhage (2 cases) and pyogenic meningitis (1 case), which is comparable to Sane M et al., findings of four cases of subarachnoid haemorrhage, two cases of meningitis, two cases of intracerebral haemorrhage, and two cases of cerebral abscess with meningitis [6]. In Narsireddy R et al., study, central nervous system causes of sudden death included two cases of subarachnoid haemorrhage, one case of intracerebral haemorrhage, two cases of epilepsy, and one case of superior sagittal venous thrombosis [2].

Author's name, Place/year of study	Least common system involved	Second least common system involved
Sane M et al., [6] (N=159) (Aurangabad, India) (2013)	Genitourinary system (3.1%)	Miscellaneous (3.1%) (Septicaemia anaemia, Cerebral malaria, Diabetic nephropathy)
Khan DF [10] (N=108) (Bangladesh) (2019)	Genitourinary system (2.77%)	Gastrointestinal Tract (GIT) (4.62%)
Nofal HK et al., [1] (N=223) (Saudi Arabia) (2011)	Sickle cell disease and G6PD deficiency (0.9%)	Renal disease (3.1%)
Present study (N=430)	CNS (0.46%)	Genitourinary system (0.94%)

[Table/Fig-19]: Comparison of histopathological spectrum of least common finding of sudden death cases [1,6,10].

In the present study, a total of 12 cases of sickle cell disease were identified. Among them, cirrhosis was found in two cases. One case of sickle cell disease presented with subdural haemorrhage and ischaemic heart disease, while nine cases showed ischaemic heart disease with sickle cell disease. These findings are comparable to Joshi C study, which identified six cases of sickle cell disease involving blood vessels with vaso-occlusion of the small vessels of the heart [8]. Sickle cell disease, causing vaso-occlusive haemoglobinopathy, can lead to myocardial infarction. In Mancini EA et al., study (2003) in Puducherry, India, myocarditis was found in 3.3% of cases, myocardial microinfarction in 20%, and congestive heart failure in 9.9% of cases of sickle cell disease [15].

Limitation(s)

In cases of sudden death, causes other than limited organs such as the heart, lungs, liver, spleen, kidneys, and brain, such as gastrointestinal or pancreatic causes, may not have been identified. Since authors were unable to examine the organs in a fresh state, diseases like pulmonary embolism might have been missed.

CONCLUSION(S)

In the present study, authors observed a striking number of sudden natural deaths. Cardiac causes contributed to the major cause of sudden death, posing a health concern in our society. Atherosclerosis is the main culprit in causing myocardial infarction. Sudden death is an issue of concern, and a meticulous postmortem and histopathological examination are necessary to ascertain its cause. The population should be educated about annual health check-ups for early diagnosis and treatment of avoidable diseases. Modifiable (acquired) risk factors like hypertension, smoking, tobacco chewing, and alcoholism can be reduced through health education, counselling, and medical treatment. With the help of an easy and fast transport system, trained professionals, and affordable emergency medical services, sudden death cases can be decreased.

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