

# SUDDEN NATURAL DEATHS AMONG ADULTS AND CARDIAC PATHOLOGY- EVALUATION OF GROSS POSTMORTEM AND HISTOPATHOLOGY FINDINGS

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*Abstract- The causes of sudden cardiac death are diverse, and are a function of age. In adults, coronary atherosclerosis and acquired forms of cardiomyopathy, Cardiac arrhythmia, myocardial infarction are the most common findings at autopsies of sudden cardiac death. Almost all sudden cardiac death investigations require correlation of circumstantial data with autopsy and laboratory data. A complete autopsy, including detailed neuropathological and cardiovascular examination with toxicological studies, must be performed in the context of all available clinical information and of the circumstances of death, thus excluding noncardiac causes and discovering those that are cardiovascular in origin but not related to coronary causes. A detailed protocol is presented for a practical use in suspected cases of sudden cardiac death. Histology may offer structural details of the cardiac wall and coronary intraluminal changes, particularly when serial section studies are performed. Although some techniques have considerable merit in the research setting, many factors limit their application in daily forensic autopsy practice, particularly when autolysis is present. The possibility that immunohistochemical and biochemical methods, quantitative morphometry, and demonstration of apoptosis in the myocardium might enhance the detection of the early cardiac changes in sudden cardiac death is an exciting field of research. Most of the biochemical analyses were carried out immediately post extraction. This study was conducted at Department of Forensic Medicine. Totally 100 cases were studied. Post mortem (PM) study was carried out in clinically suspected / confirmed cases of MI. It is found that in majority of the cases died of MI.*

**Keywords-** Cardiomyopathy , immunohistochemica ,noncardiac

## INTRODUCTION

SCD is natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms. Preexisting heart disease may or may not have known to be present, but the time and mode of death are unexpected. If the death is unwitnessed the definition is used for a person known to be alive and functioning normally 24 hours before being found dead.

## CAUSES OF SUDDEN CARDIAC DEATH

**Angina pectoris** is a form of heart disease in which the sufferer feels pain and tightness in the chest because of brief or partial blockages of oxygenated blood to the heart. It typically occurs under exertion resulting in an increased demand for oxygenated blood that cannot be met adequately by diseased coronary arteries, thus leading to ischemia (restriction in blood supply). Angina pain typically leads to a pressure like sensation in the chest. Medical therapy for angina is directed at decreasing myocardial oxygen demand, increasing myocardial blood flow, or both. A large number of drugs are used to treat angina. Surgical and interventional cardiology procedures include angioplasty and coronary artery bypass graft surgery (CABG).

**The cardiac arrhythmias** consist of abnormality of cardiac rhythm and heart rate. A heart rate between 60 and 100 beats per minute is arbitrarily defined as a normal sinus rhythm, and any disturbance from this is defined as arrhythmia. Broad categories include disorders that cause slow ventricular heart

rates (bradycardia, with rates of fewer than 60 beats/minute) and fast ventricular heart rates (tachycardia, with rates of more than 100 beats/minute).

**Cardiac arrest** denotes the functional cessation of the pumping action of the heart. Sudden cardiac arrest usually results from severe disturbance of cardiac impulse generation or conduction, which causes cardiac output to fall to levels that cannot sustain cardiac function. Studies show that of every 100 patients who experience an out of hospital cardiac arrest, only 15 survive (Osborn, 1996).

**Myocardial infarction (MI)** or acute myocardial infarction (AMI), commonly known as a heart attack, occurs when the blood supply to part of the heart is interrupted causing some heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery which carry blood from the heart to the body parts, following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (like cholesterol) and white blood cells (especially macrophages) in the wall of the artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage and/or death (infarction) of heart muscle tissue (myocardium). Classical symptoms of acute myocardial infarction include sudden chest pain which may radiate to the left arm, jaw, teeth, and throat, shortness of breath, nausea, vomiting, palpitations, sweating, and anxiety (often described as a sense of impending doom). Women may experience

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fewer typical symptoms than men, most commonly shortness of breath, weakness, a feeling of indigestion, and fatigue. The symptoms usually begin at a low intensity, increase over 2 to 3 minutes and become severe and more persistent.

### **Incidence of Sudden Cardiac Death**

In western countries about two thirds of all natural sudden deaths in the general population are cardiac related (29, 30). Of all cardiac related deaths 50 % or more are classified as SCD. In an analysis of mortality data from 1989 to 1998 in the United States, SCD increased in proportion to all cardiac deaths from 56 % to 64 %. The age-adjusted decline in SCD rates was 11.7 % in men and 5.8 % in women. During that period there was a 21 % increase in age-specific death rates for SCD among women aged 35 to 44 years . In the United States 460,000 died of SCD during 1999 (31) with CAD as the major cause.

The incidence of SCD in the general population is approximately 1/1,000 inhabitants per year (32, 33). In a register study from northern Sweden in persons aged 35-64 the incidence was 0.65/1,000 in men and 0.12/1,000 in women. The SCD incidence decreased significantly among men but not among women during the study period 1985-1999 . Various estimates exist for the magnitude of sudden cardiac death in the general population of the United States. Figures based on primary cardiac arrest from first responder agencies and from death certificate data give estimates ranging from 184,000 to greater than 400,000 per year. Thus in the general population of the United States the incidence of sudden cardiac death is about 1 death per 1000 head of population per year and as described below this figure holds for other developed nations.

A prospective cohort study using an integrated primary care database in the Netherlands reported an annual incidence of sudden out of hospital cardiac arrests of 0.92 cases per 1000 person-years (95% Confidence interval (CI): 0.85, 0.99). The study population comprised 249,126 subjects with a mean follow up of 2.54 years. In this period 4,892 deaths were identified, 582 of which were classified as (probable) sudden cardiac death .

It has been estimated that in the developed world sudden cardiac death is the largest cause of natural death accounting for 12-18% of total mortality and 50% of cardiac mortality. These figures are based on retrospective studies that may be an over-estimate as described below. Sudden cardiac death accounted for 5.6% of the annual mortality of a population of 660,486 residents of Multnomah County, Oregon according to a prospective study .Between 1 February 2002 and 31 January 2003, 353 residents suffered sudden cardiac death (incidence 53 of 100,000, median age 69 years, 57% male).

The incidence of SCD is higher in men than in women, with men two to four times more affected than women when age is adjusted for. Most studies of primary cardiac arrest have reported a threefold higher incidence in men compared with women but these studies have looked at data retrospectively. Prospective studies may reduce the sex discrepancy as shown in a study that found 43% of 353 sudden cardiac death cases were female. A prospective study in the Netherlands that classified 582 people as having

probable sudden cardiac death estimated the risk to be 2.3 fold higher in men than in women.

### **METHODOLOGY IMPORTANCE OF AUTOPSY**

Autopsy report is important because it is the most practical reflection of the level of health in populations. It provides the basis for testable hypotheses concerning the determinants of variation of the causes of death. These determinants are used to define health problems, to identify the emerging problems of public health and to monitor the efficacy of health programs. Thus, autopsy report has a crucial role to play in strategic health planning. In the India, there is a legal requirement to record deaths. Thus, the advantage of mortality statistics over other statistics relating to health is that they are more generally available. Critically, their validity depends on their completeness and accuracy.

This study was conducted at Department of Forensic Medicine. Totally 100 cases were studied. Post mortem (PM) study was carried out in clinically suspected / confirmed cases of MI. In addition 3 cases (1 case of fall from height, 1 case of dehydration and 1 case of hypertrophic obstructive cardiomyopathy) of sudden death due to other causes were also included in the study as negative control. To accomplish the goal, a detailed proforma was designed. This proforma consisted of two parts.

Part I was to be completed by the pathologists of institute, who conducted initial postmortem

examination. The information was collected from attendants and medical case history sheets. This part included all particulars of the deceased, physical activity prior to episode, any previous sick report, smoking habit, any prodromal signs and symptoms, time lapse between onset of symptoms and death, results of any investigations, any pathology in organs other than cardiovascular system or any other relevant finding. About time lapse between onset of symptoms and death, an eyewitness was consulted if needed.

Part II of the performa was also completed at Pathology lab where unopened hearts along with other vis- viscera were received .These specimens belonged to patients who admitted at city hospital. Each heart was examined by a senior pathologist and following parameters were assessed: Weight of heart, ventricular surface fat and thickness of fat at base of right coronary artery, apparently dominant artery, coronary atherosclerosis, thrombosis, occlusion and its site from origin of vessel, state of coronary ostia, recent/old infarcts along with their size and location. The coronary arteries were examined by transverse cuts at 2-3 mm intervals all along their length. The lesions of atherosclerosis were visually categorised as:

I - Artery appeared grossly normal but had microscopic findings of atherosclerosis.

II - Thickening of vessel wall with 25 to 50% narrowing of lumen.

III- Thickening of vessel wall with 50 to 75% narrowing of lumen.

IV - Thickening and calcification with more than 75% narrowing of lumen.

Coronary artery dominance was assessed by noting the origin of posterior descending branch from either right or left artery. Representative sections were taken from all coronary arteries. The hearts were then opened by modified Virchow's method following the direction of blood flow. All the chambers were washed off any blood clots and examined for any pathology of valves or endocardium. Thickness of ventricular walls and interventricular septum was also measured. Blocks for histopathological examination were taken from right atrium, SA node, AV node, base and middle of septum; anterior and posterior walls of both ventricles and from left anterior and posterior papillary muscles. Serial sections were taken from areas of infarcts if any. These tissues were processed in automatic tissue processor "SAKURA - JAPAN" for 16- 18 hours. Three to five micron thick sections were made with the help of manual microtome "LEITZ - GERMANY".

The pathologist has a unique opportunity to study SCD resulting from all manner of cardiac diseases. Myocarditis, cardiomyopathies, coronary artery and other congenital anomalies may be identified. However, there is occasional doubt as to the true cause of death in patients with SCD. There probably is nothing more frustrating for the pathologist than to perform an autopsy and come up with no significant findings.

The four steps in the investigation of a sudden death are (1) obtaining the history and scene information, (2) performing a gross and microscopic autopsy, (3) performing appropriate laboratory tests, and (4) making the diagnosis. When examining the heart grossly, it is important to preserve the anatomic landmarks, section the coronary arteries closely, and recognize lethal abnormalities such as anomalous origin of the coronary arteries. Specimens useful for toxicologic analysis include whole blood, serum, vitreous humor, gastric contents, bile, urine, a purple top tube of blood, and frozen myocardium and spleen.

A complete autopsy, including detailed neuropathologic and cardiovascular examination with toxicologic studies, must be performed in the context of all available clinical information and the circumstances of death. The dissection of the heart can be practiced in different ways, but we have adopted the inflow-outflow method: the cut follows the direction of the blood flow from the caval veins on the right side of the heart to the pulmonary trunk and pulmonary artery. On the left side, the atrium is opened by cutting the pulmonary veins, and the cut is continued with the dissection of the left side of the infundibulum and of the aorta. To examine the coronary arteries, different methods that are more or less complicated have been introduced.

#### **MOLECULAR DIAGNOSIS OF SUDDEN CARDIAC DEATH DISEASES**

With the explosion of molecular techniques, deoxyribonucleic acid (DNA) testing on peripheral blood and tissue has revolutionized the diagnosis of genetic causes of sudden death. We describe the basic methods of tissue preparation and DNA analysis as a useful overview for the clinical pathologist.

#### **Collection of Deoxyribonucleic Acid from Blood Samples**

It is easiest to amplify DNA that will be used for genetic testing when the DNA is taken from blood samples. Ideally, at the time of autopsy the coroner or pathologist collects 15 ml of blood in several tubes containing ethylene di aminetetraacetic acid (EDTA), which prevents coagulation and degradation of the DNA. The tubes are stored at 4°C until the DNA is extracted for analysis, which should be within 1 week, although sometimes we have extracted DNA 4 months after collection. If the blood samples are collected in tubes that do not contain an anticoagulant, the DNA should be extracted promptly (within days of the initial collection).

#### **RESULTS**

The study comprised of 100 cases that were brought to the Department of Forensic Medicine, for Medico legal autopsy during the period of Aug. 2009 to Aug. 2011. Cases showing signs of decomposition were not considered. Cases of sudden unexpected deaths with history suggestive of heart disease were especially included. Detailed histories regarding the circumstances leading to death, any past history of myocardial infarction, or symptoms suggestive of heart disease like breathlessness, chest pain, collapse, were obtained from the relatives, inquest papers and wherever possible from the hospital records. In none of the cases ante mortem diagnosis of myocardial infarction was made (that presented as sudden death). Either the patient was found dead or was declared in the hospital as "brought dead".

The commonest symptoms in order of their frequency were: chest pain 58%, sudden collapse 50.0%, dyspnoea 42%, cold sweating 16% and vomiting in 14% cases. Majority of the cases died at rest whereas 10 died during moderate to severe exertion. Electrocardiography could be done in 5 individuals only, which revealed ventricular fibrillation and asystole. In 76% of the cases posterior descending artery originated from right coronary artery. Most of the cases revealed triple vessel disease followed by double vessel disease (15 cases) and single vessel disease (10 cases). The predominant involvement was seen in left anterior descending artery (LAD) followed by right coronary artery, left circumflex coronary artery and left mainstem coronary artery. Most common cause of sudden cardiac death was coronary atherosclerosis found in 52 cases (79%). Lipid rich atheromata were found in 65% and fibrofatty atheromata in

35% of cases. Atherosclerotic coronary occlusion alongwith thrombosis was found in 37 cases (56%), out of which 30 (45%) revealed recent thrombosis with plaque rupture and erosion as a substrate.

Recent and old infarcts were seen in 20.8% and 35.1% cases respectively. Conduction system of the heart showed necrosis of SA and AV nodes in one and two cases respectively due to narrowing of nutrient arteries. Only one case revealed nonspecific fatty infiltration in Bundle of His. Both symmetric and asymmetric hypertrophic (increased thickness of left ventricular wall and interventricular septum) was seen in 5 cases. In two hearts interstitial lymphocytic infiltrate (myocarditis) was observed.

Sixteen cases of traumatic sudden deaths were included as controls. The age range of these cases was 21 to 50 years. Three of such cases showed mild degree of atherosclerosis in LAD. None of them revealed signs of thrombosis or recent and old myocardial infarct. In one case only, fatty infiltration thrombosis or recent and old myocardial infarct. In one case only, fatty infiltration was seen in the A-V node.

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