

Searching cause of death through different autopsy methods: A new initiative

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ABSTRACT

A lawful disposal of human dead body is only possible after establishment of proper and valid cause of death. If the cause is obscure, autopsy is the only mean of search. Inadequacy and unavailability of health care facility often makes this situation more complicated in developing countries where many deaths remain unexplained and proper mortality statistics is missing, especially for infant and children. Tissue sampling by needle autopsy or use of various imaging technique in virtopsy have been tried globally to find out an easier alternative. An exclusive and unique initiative, by limited autopsy through tissue biopsy and body fluid analysis, has been taken to meet this dire need in African and some of Asian developing countries, as worldwide accepted institutional data are even missing or conflicting at times. Traditional autopsy has changed little in last century, consisting of external examination and evisceration, dissection of organs with identification of macroscopic pathologies and injuries, followed by histopathology. As some population groups have religious objections to autopsy, demand for minimally invasive alternative has increased of late. But assessment of cause of death is most important for medico-legal, epidemiological and research purposes. Thus minimally invasive technique is of high importance in primary care settings too. In this article, we have made a journey through different autopsy methods, their relevance and applicability in modern day perspective considering scientific research articles, textbooks and interviews.

Keywords: Cause of death, conventional autopsy, minimally invasive autopsy, virtopsy, mortality statistics

Introduction

Death, the ultimate fate of human's life, ends with lawful disposal of the body with proper and valid cause of death. If the cause of death is unknown or if the death is sudden, suspicious, unnatural death a thorough and scientific investigation is necessary. Autopsy or postmortem examination is gold standard in this respect from ages to find the cause of death and to study diseases.

In 15th and 16th centuries, autopsy was considered a mystical and religious issue. Later on, the scientific relationship between clinical manifestations and autopsy findings was fully established.^[1]

An invasive autopsy by opening all the body cavities represents the traditional means of postmortem investigation in humans.

Body fluid aspiration study with various tissue biopsy analyses have been tried to supplement and ultimately replace, if possible, the traditional method of late. With the advancement of medical fraternities, modern cross-sectional imaging modalities such as computed tomography (CT) scan, magnetic resonance imaging (MRI), etc., have been implemented with successful prospect.^[2]

Autopsy, thus considered as the tool for research of evolution of disease and causative agents and organisms, reflects the cellular basis of the disease evident on architectural alterations of the cells and tissues.

Global Perspective of Cause of Death

Global malaria deaths increased from 995,000 in 1980 to a peak of 1,817,000 in 2004, decreasing to 1,238,000 in 2010. In Africa, malaria deaths increased from 493,000 in 1980 to 1,613,000 in

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2004, decreasing by about 30% to 11,33,000 in 2010. Outside of Africa, malaria deaths have steadily decreased from 502,000 in 1980 to 104,000 in 2010.^[3]

Mortality data as per International Classification of Disease-10 in South Africa in 2007 shows 93.9% ill-defined and unknown causes of mortality in 2007, and childhood mortality contributed to more than 11% of all deaths, of which 32.2% are at home, and 2.5% are brought dead at health centers. Natural deaths, mentioned as 10 times more in occurrence than unnatural causes, have single cause in 60.3% and two combined causes in 26.6%.^[4]

Statistically and explainably higher childhood mortality is seen among lower socioeconomic groups of developing countries due to most obvious mortality determinants including malnutrition, infections, maternal factors, and health-care facility available and disbursed. It obviates the magnitude of inequality varies between countries and over time, suggesting its amenability to intervention. An intervention to reduce inequalities in childhood mortality would substantially improve population health to reaching the millennium development goals.^[5]

Maternal mortality is another challenge to healthcare setup worldwide. A database of 2651 observations of maternal mortality from 181 countries for 28 years (1980–2008) revealed 342,900 maternal deaths worldwide in 2008, down from 526,300 in 1980. The global maternal mortality ratio (MMR) decreased from 422 in 1980 to 320 in 1990 and was 251/100,000 live births in 2008. The yearly rate of decline of the global MMR since 1990 was 1.3%. During 1990–2008, rates of yearly decline in the MMR varied between countries, from 8.8% in the Maldives to an increase of 5.5% in Zimbabwe. More than 50% of all maternal deaths were in only six countries in 2008 (India, Nigeria, Pakistan, Afghanistan, Ethiopia, and the Democratic Republic of the Congo).^[6]

With advancement of various fields of medical science worldwide, forensic and pathological autopsy also gained its superiority in technique and interpretation. The cause of death determined after autopsy plays a pivotal role in epidemiological research and analysis leading to public health-related decisions and policy making. It also contributes to study the pathological process, treatment protocol, complications, genetic research, and also in the audit of medical practice. In 1999–2000, the National Confidential Enquiry into Perioperative Deaths in the United Kingdom showed 23% postoperative deaths had major discrepancies in the form of inconsistency between pre- and post-mortem diagnosis. Any mortality data not established and justified through autopsy are better not to rely upon blindly.^[1]

A study of clinic-pathologic analysis by autopsy in Mozambique on maternal death showed 40.3% major diagnostic errors. A high rate of false-negative diagnoses was observed for infectious diseases, namely, HIV/AIDS-related conditions (33.3%), pyogenic bronchopneumonia (35.3%), pyogenic meningitis (40.0%), and puerperal septicemia (50.0%). Eclampsia was main source of false-positive diagnoses.^[7]

In a systemic review of 53 autopsy series, 42 detected major errors and 37 reported class I errors. Totally, 26 autopsy series revealed both major and class I error rates. The median error rate for major errors and for class I errors was 23.5% and 9.0%, respectively.^[8]

Is Needle Autopsy an Option for Minimally Invasive Autopsy?

Infants and children along with adult population showed a significant decrease in autopsy rate worldwide in recent time. Question arises regarding the actual success of traditional autopsy methods. Hence, minimally invasive autopsy (MIA) technique through needle biopsy of organs becomes an option for valid reason since it maintains integrity of the body. Needle autopsy is not a new discovery. Terry, almost 70 years back, discussed the benefits of needle autopsy and performed to diagnose with 92% success rate. Its advantages include avoiding reluctance of relatives of deceased for consenting autopsy, least disfigurement of the body, requirement of less instrumentation and much less time, and cost of the whole procedure. It only requires a wide bore trocar and cannula attached with a suction device or piston to be inserted through tissue space for the collection of tissues, for example, liver, lungs, spleen, kidneys, brain and even pancreas, suprarenal, etc., for the analysis of pathology and possible cause of fatality. However, many times, the etiology remains unrevealed as in generalized infections, peptic ulcer and its complications, intestinal perforation or obstruction, many vascular disasters, and some cardiac conditions which are tough to find with tissue biopsy only. The limitation is insufficient tissue sampling and missing of the exact location of pathological site as being anatomical surface marking based technically skilled blind procedure. It is mostly helpful in known space occupying lesion or enlarged viscus. Often the samples are damaged for which the instruments have been improvised with time.^[9]

Various imaging methods have been tried in recent past through ultrasound-guided, laparoscopy-based techniques, but was not much convincing and it needs further detailed study.^[10]

Some groups refer ultrasound guidance yields a significantly higher success in heart and left kidney. The success largely depends on the experience of the operator and the particular organ involved.^[11]

A retrospective needle biopsy study on 394 biopsies performed between 1948 and 1968 by 32 different pathology residents in the United States revealed success rates ranged from 34% for the kidneys to 92% for the liver.^[12] CT-guided percutaneous needle biopsy has been used and showed good prospect is expected in future. Even combined approach based on postmortem MRI (PM MRI) and endoscopic autopsy with tissue biopsy have been tried in recent times and found effective with minimal cosmetic consequences.^[13]

Minimally Invasive Autopsy and Radiology-Virtopsy

With the worldwide modernization of noninvasive radiological interventions, imaging-based autopsy is new, emerging, promising, and least invasive of the lot. It is claimed to be an alternative to conventional autopsy by the pro-group scientists. It has given rise to the term “VIRTUAL AUTOPSY” (Latin word virtus meaning “useful, efficient and good”) or the combined term as “VIRTOPSY”. Multi-section CT, micro-CT, MRI, magnetic resonance microscopy, photogrammetry-based three-dimensional (3D) optical scanning are applied chiefly to diagnose the cause, mode, manner, and even circumstance of death. Additional minimally invasive angiographic technique augments the diagnostic efficiency further. More advanced and highly digitalized modalities such as 3D color encoded surface scanning and fusion of cross-sectional two-dimensional and 3D surface scanning data are supplements. Chief advantages are of being quick, reproducible, observer independent, less contaminating, and noninvasive. Disadvantages mainly include very high cost, highly mechanized, and instrument-based procedure, inability to interpret infection status, color changes, and artifacts. Moreover, morphological data and variation of signal intensity characteristics in case of ante- and post-mortem data are yet to be studied, revealed, and established. The scheme proposed by Dirnhofer *et al.* in 2006 is depicted^[2] in Figure 1.

Modern MIA is a combination of whole-body CT and MRI and guided 12-gauge needle biopsy of surface of brain and meninges, upper and lower lobes of the lung, right and left heart ventricle, right and left lobe of the liver, both kidneys, adrenal glands, pancreas, and spleen with the right and left lobe of the thymus, added in children.^[14]

A fetal autopsy-based study of 44 cases using PM MRI and percutaneous biopsy showed 47.7% diagnostically comparable and 72.7% clinically significant result in comparison to conventional autopsy.^[15]

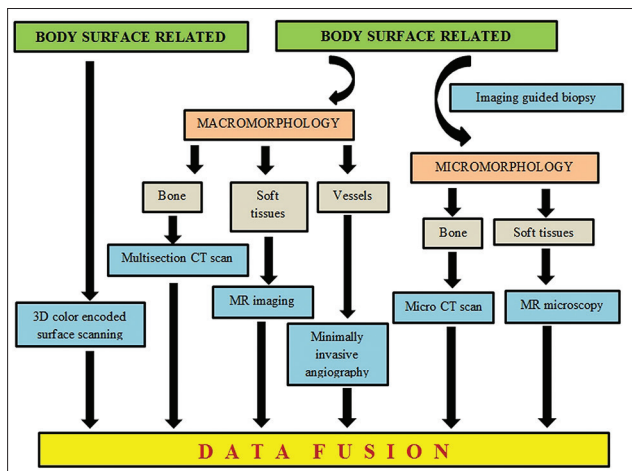


Figure 1: Scheme of virtual autopsy procedure

Initiative of Gates Foundation: Search for the Reality

To reduce the mortality rate in the childhood, a present day proper worldwide public health data are needed to combat any next epidemic. As per Bill Gates, over the past 15 years, deaths of children in developing countries have been reduced substantially. The prevention of spread of disease and spot emerging epidemics can also be achieved by MIAs.^[16]

The World Health Organization (WHO) and the Institute for Health Metrics and Evaluation (IHME) in Seattle, Washington, separately estimated deaths due to malaria in 2010. The WHO calculated 655,000 deaths and IHME counted almost double, i.e., 1.24 million. There also lies significant variation in counting mortality data as below which establishes the need more prominently [Figure 2].^[17]

Almost 70% of world’s population lives and dies in countries having poor functional vital systems of birth and death registration. There most deaths occur outside of medical facilities and are neither enumerated nor classified by cause.^[18,19] An autopsy-based study in 2005 and 2014 showed wrongful issue of death certificated by the attending doctors in one-third and one-half of the total cases, respectively. The later one was conducted in India.^[17]

Moreover, developing countries lack the money and materials for autopsies. Some African countries have very poor number of pathologists. Many people fear and mistrust the idea of dissecting open a corpse, which compels verbal autopsies to be performed which has serious drawbacks such as recall bias and cultural ritualistic believes with ambiguous symptoms—fever, diarrhea, and cough.

One of the major factors for the failure to perform the traditional autopsy is due to its high cost. To reduce the cost of that (average \$500 in full autopsy) Gates Foundation has adopted one protocol

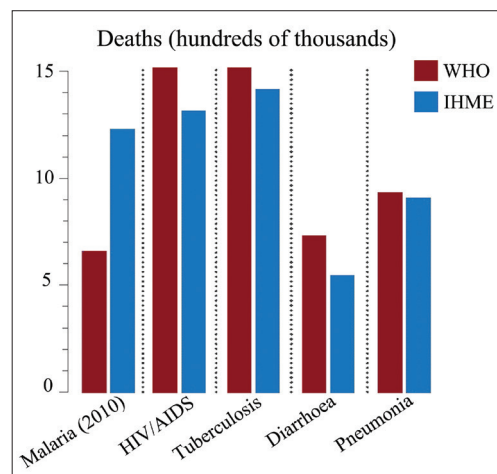


Figure 2: Mortality statistics: The World Health Organization versus Institute for Health Metrics and Evaluation

of tissue biopsy and body fluid sampling analysis under imaging guidance which will bring down the expenditure to an average \$200 to \$400 per case only.^[20] A sum of \$2.3 million granted over 3 years to compare MIA with traditional dissection method in 260 cases in Mozambique divided into four cohorts – neonates, children, adults, and pregnant women under the guidance of Dr. Quique Bassat, a pediatrician at Barcelona Centre for International Health Research in Spain and an additional 60 cases in Brazil as a partner study. Analysis of the following will be done in each case to find the cause of death: (a) Cerebrospinal fluid, (b) blood, (c) liver, (d) lungs, (e) bone marrow, (f) brain, (g) kidney, (h) spleen, (i) rectal swab [Figure 3].^[17]

However, this also has raised controversies as pathologists in Mozambique are skeptical that mere chunks of tissue can provide mortality data. To make MIAs acceptable, a second, anthropological and funeral practice study is going on in Mozambique, Kenya, Gabon, Mali, and Pakistan. In Gabon, elders objected doctors to insert even a needle in adolescent dead body who had not gone through sex-initiation rites. Some sects believe that the dead feel pain. A separate MIA project by the International Centre for Diarrheal Disease Research in Dhaka, Bangladesh, revealed strong taboos against autopsies in Muslim countries as they bury people before sunset (the day they die) and autopsies can delay that. Muslims also wash the body after death, at which point doctors cannot touch it. Despite these taboos, Muslim leaders supported MIAs once they observed MIAs. Thus, MIA is also contributing social-science research along with clinical work. Although preliminary, the results look promising. On the social science side, interviews revealed a high theoretical acceptance rate, around 80%.^[17]

Nonphysicians are also being trained as MIA technicians to serve rural areas for the collection of samples. Even mobile MIA clinics, old converted ambulances with self-contained and self-cleaning units in back, are also being employed. Ultimately, scientists and health officials want to spread MIAs across the globe. Gates Foundation has also launched a 20-year surveillance program called Sentinel Epidemiology and Etiology

Data (SEED) in April 2015. Gates Foundation will support the project with \$75 million over first 3 years, and \$75 million more coming from other sources. SEED will open sites in roughly 25 places in Africa and Asia, some by 2018, and MIAs will be the procedure of choice.^[21] The aim of the SEED is to perform MIAs on at least 20% of deaths in each region focusing on children at first and adults later.^[17]

Another team based long-term initiative, i.e., Child Health and Mortality Prevention Surveillance Network, or CHAMPS, has been launched to provide information for assessment and prioritizing the measures taken. It is led by the Emory Global Health Institute, in collaboration with International Association of National Public Health Institutes, US Centers for Disease Control and Prevention, and the Task Force for Global Health.^[22] This service will cater six locations in Sub-Saharan Africa and South Asia at first, then gradually will be spread over twenty locations.^[23] Field workers will be employed to take biopsies of children to search for the cause of death after laboratory investigations. New outbreaks can be found and taken care into with this surveillance system.^[24]

Prospects of the Initiative

Dilemma of kin consenting autopsy is hurdle toward implementation and results refusal originating from diverse complex interaction of sociocultural factors. A study detected that various religious beliefs like neonates should not be autopsied, dead neonates are taboo and punishment by Gods for past wrongdoings influenced 46.8% consenting authority.^[25]

In Zambia, refusal rate for child autopsy was 75.4%, reason being 43% as “time wastage,” as 25% as already death certificates issued and arrangements for disposal made, 8.6% as ancestral spirits forbade mutilation of dead bodies.^[26]

The WHO reported 34% mortality of population below 14 years age in low-income countries in 2002. Mostly affected are sub-Saharan Africa, then South Asia, East Asia, and Northern Africa. A diverse international group of 1000 people comprising women, men, and children from all over globe died in 2002 is taken; low-income countries contribute 501 of them. Only 22% all people reach 70 years of age in low-income countries. Although cardiovascular disease is leading cause of death, infectious diseases (HIV/AIDS, lung infections, tuberculosis, diarrheal diseases and malaria) claim substantial lives. Pregnancy-related complications and childbirth are major cause of fatality to infants and mothers.^[27]

Hence, the cohorts chosen for surveillance is justified and materialistic as perinatal and pediatric autopsy for proper diagnosis of cause of death can be valuable in terms medical knowledge, mortality, and clinical data. Confirmation or rejection antemortem pathology related to specific diagnosis, if any, can be achievable. It remains the final and many times the only mean to confirm genetic and obstetric disorder. MIAs are quicker, potentially cheaper, and cleaner in this aspect.

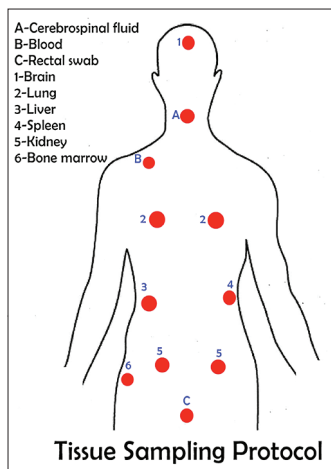


Figure 3: Tissue sampling protocol

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Conflicts of interest

There are no conflicts of interest.

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