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REVIEW ARTICLE

Molecular Forensic Medicine: An Overview

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Abstract

Molecular autopsy or Molecular Forensic Medicine is gaining importance across the globe in both developed and developing countries. This is relatively less thought-out or discussed in the Indian scenario. We are attempting to present a mini-review of ongoing developments in the field of Molecular Forensic Medicine and emphasize the need for starting Molecular autopsy programs in Medico-Legal Centres in our country. This cross-disciplinary branch requires concerted efforts from various stakeholders for successful implementation in day-to-day autopsy practice. In the post-pandemic era, it is worth noting that most of the leading teaching hospitals in India now possess the necessary infrastructure to carry out molecular studies. This presents a unique opportunity for us to initiate our national molecular autopsy program.

Keywords: Molecular Autopsy, Thanatotranscriptome, Thantomicrobiome, Sudden Death, Thantomarkers, Regenerative Medicine, Transplant Medicine, Forensic Pharmacogenomics, Toxicogenetics

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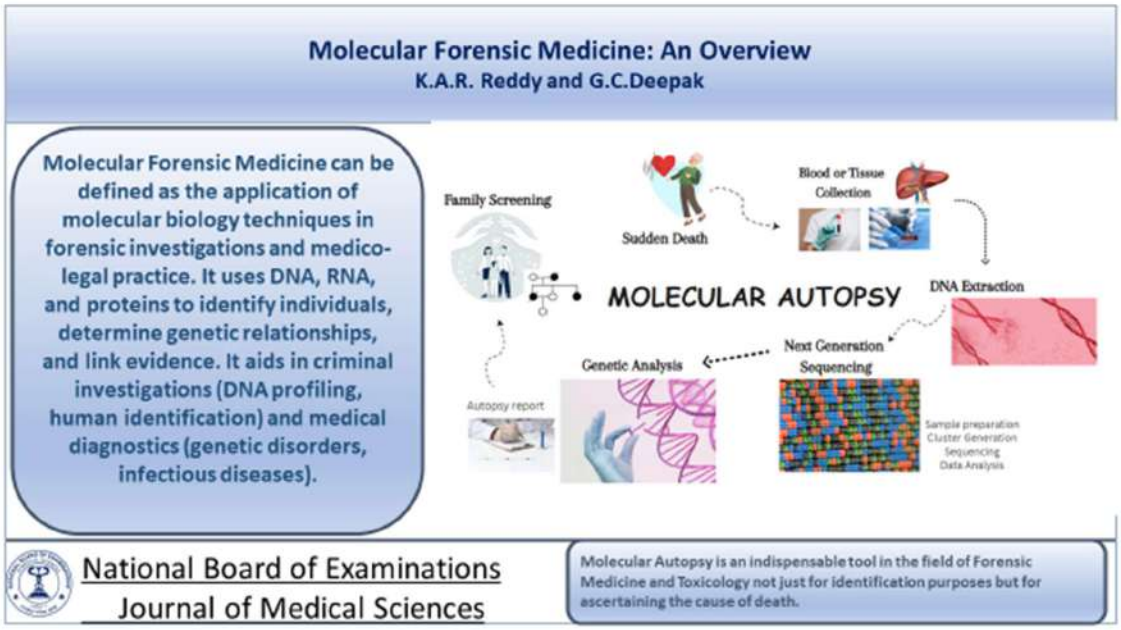
Graphical Abstract



Introduction

According to the National Cancer Institute, USA, Molecular Medicine is a branch of medicine that develops ways to diagnose and treat disease by understanding the way genes, proteins, and other cellular molecules work. Molecular medicine is based on research that shows how some genes, molecules, and cellular functions may become abnormal in diseases like cancer Molecular Forensic Medicine is defined as the application of knowledge of the field of Molecular Medicine in the aid and administration of justice.

Review of Literature

Molecular medicine is a hybrid branch with close collaboration between physicians and biologists. As we live in a promising world of personalized medicine, every medical practitioner needs to have a basic idea of recent trends in the field of molecular medicine. However, in this article, we are restricting ourselves only to the applications of this field towards Forensic Medicine and suggesting a few future directions of research.

Every forensic pathologist immediately thinks of DNA fingerprinting when someone mentions molecular techniques. A thorough assessment of the literature revealed numerous recent advancements in the area of molecular forensic medicine that go beyond the field's conventional uses for identification in resolving medico-legal cases. However, molecular testing is currently being considerably used and has far more potential in the field of autopsy. Today, the autopsy pathologist can analyze molecular data for inheritable thrombophilias, hereditary heart disorders, pharmaco-genetics, and infectious agent detection. The vital data gleaned from these genetic tests is frequently crucial to the immediate relatives of the dead as well as the community at large and may have significant medico-legal implications [1].

Molecular research has discovered mutations for structural cardiomyopathies

(myosin, troponin) and electrolyte channels (sodium, chloride, calcium) that have helped to understand these disorders. Molecular studies are of great help for the autopsy surgeon in cases of the sudden death of children and situations where structural alterations in the heart during autopsy are not obvious.[1] Six important cardiac ion channel genes (KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, and RyR2), for which disease-causing sequence variations have been previously described, are routinely included in the molecular analysis for cardiac channelopathies [2,3] (Table 1).

A rising number of inherited and congenital arrhythmia illnesses are brought on by gene mutations that produce faulty ionic channel proteins that control the transit of sodium, potassium, and calcium ions across cell membranes. Long QT syndrome (LQTS), short QT syndrome (SQTS), Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia (CPVT) are some of these ion channel diseases. The clinical and genetic characteristics of Brugada syndrome and the nocturnal sudden unexplained death syndrome in young Southeast Asian males are comparable [4]. Over-interpretation of excess epicardial fat in someone who is overweight or obese as evidence of arrhythmogenic cardiomyopathy and over-interpretation of hypertensive cardiac disease as hypertrophic cardiomyopathy are the two most typical cases we observe [5].

The full set of genes linked to various basic arrhythmia syndromes or cardiomyopathies is unknown. Thus, the absence of genetic variants at the time of genetic testing does not rule out the potential that a specific clinical trait has a genetic basis [5].

Table 1. Showing details of the genetic basis of sudden cardiac death in an Anato-morphologically normal heart [4].

S. No	Condition in which heart is Anato-morphologically normal	Type of disease and Genes implicated
1	Long QT Syndrome	SQTL1 KCNQ1/KVLQT1, SQTL2, KCNH2/HERG, SQTL3 SCN5A, SQTL4 ANKB, SQTL5 KCNE1/MinK, SQTL6 KCNE2/MiRP1 SQTL7 (Andersen S.) KCNJ2, SQTL8 (Timothy S.) CACNA1C, SQTL9 CAV3, SQTL10 SCN4B Jervell–Lange-Nielsen (autosomal recessive) S. JLN I KCNQ1, S. JLN II KCNE1
2	Short QT syndrome	KCNH2 (HERG, SQT1) KCNQ1 (KvLQT1, SQT2), KCNJ2 (Kir2.1, SQT3)
3	Bruguda Syndrome	5CN5A, Ankyrin binding Motif of Nav.1.5, GPD1-L, CACNA1C, CACNB2b
4	Catecholaminergic Polymorphic Ventricular Tachycardia	RyR2, CASQ2

Molecular analysis for two common hereditary thrombophilias, factor V Leiden (FVL) and prothrombin G20210A (PT), can be performed using several standard single nucleotide polymorphism detection methods [1].

Molecular analyses or probes can detect and classify a wide range of infectious agents. This is generally the domain of public health laboratories and clinical pathology, but forensic pathologists must be aware of these techniques and ensure that specimens are collected, stored, and presented properly and promptly. H1N1, Corona Virus, avian influenza, and other viruses are examples.1 Molecular approaches can be used to diagnose extremely rare illnesses such as Leber's optic neuropathy, which can have serious consequences for the next of kin [1].

Pharmacogenetics is the study of genetic differences that lead individuals to respond differently to the same pharmacological dose. Drug concentrations can differ significantly between two people of the same weight, age, and dose. The efficacy or toxicity of a medicine can be affected by genetic differences. A person's reaction to a medicine is a complex attribute regulated by various genes [1].

Individual dose adjustments based on a patient's genotype are aided by genomic polymorphisms of phase I and phase II drug-metabolizing enzymes. Polymorphisms in the cytochrome P4502D6 gene have a significant impact on the metabolism of several medicines, including the analgesics codeine, tramadol, hydrocodone, and oxycodone. Individuals differ in that they can be classified as an extensive metabolizer, a poor metabolizer, an intermediate metabolizer, or an ultra-rapid metabolizer [6].

Molecular pathology approaches can help determine not just the cause of death, but also the manner of death, for example, in the differential diagnosis of accident/suicide or even accident/homicide. This differential diagnosis may also be critical for the regulation of insurance compensations.[6] For instance, a particular dose of a drug detected in an individual's body can be the usual fatal dose which can give the picture of a suicide attempt by that person. However, if we investigate the cases from the pharmacogenomics side, he/she can have an idiosyncrasy in metabolizing that drug which could have led to the accidental accumulation of the drug that can cause death. These situations arise in the case of drugs with low therapeutic index and also drugs of abuse. Similarly, for the sake of understanding, the examination of strangulation-related biomarkers expressed in the lung during postmortem submersion cases can help differentiate between homicide (strangulation) and accident (drowning).

Molecular biology techniques have greatly increased diagnostic sensitivity, accuracy, and validity in forensic medicine, particularly in the field of identification (paternity testing, stain analysis). For more than a decade, these techniques have been used in forensic medicine for a variety of purposes, including determining the cause and manner of death, tissue identification using mRNA and microRNA, examining gene expression levels (survival time, time since death, cause of death), and toxicogenetics [6].

Combining immunohistochemistry with relative mRNA quantification of multiple biomarkers provides valuable insights into the cause of death. In particular, SP-A (Pulmonary surfactant-

associated protein A), MMPs (matrix metalloproteinases), ICAM (intercellular adhesion molecule), CLDN (claudin), and AQP (aquaporin) are important biomarkers identified in the research.

In the investigation of pulmonary alveolar damage using MMPs, ECM, ICAM-1, CLDN, and AQPs, the up-regulation of these markers was observed in cases of sharp instrument injury and hyperthermia. Immunohistochemistry revealed increased levels of MMP-2 and -9. Notably, AQP-5 demonstrated a distinction between strangulation and smothering or choking. Immuno-staining of AQP-5 displayed weakly positive results in a linear pattern in type 1 alveolar epithelial cells during smothering and choking. Conversely, cardiac and brain injury deaths exhibited marked positivity, while most strangulation cases displayed AQP-5-positive granular aggregates and fragments within intra-alveolar spaces. Smothering and choking had lower AQP-5 gene expression compared to other groups.

Regarding cardiac strain, atrial and brain natriuretic peptides (ANP and BNP) increased in pericardial fluid. These peptides showed varied patterns depending on the cause of death. In hypothermia cases, both ANP and BNP levels were high, whereas hyperthermia led to elevated ANP levels, and chronic heart failure resulted in increased BNP levels. However, gene expressions of ANP and BNP were low in hyperthermia, similar to sedative-hypnotic intoxication [7-9].

Human postmortem microbiome research has shown that these communities exist in the host ante mortem or colonize the body after a human or animal surrogate dies. The thanatomicrobiome is the entire assemblage of microorganisms (e.g., bacteria and fungus) discovered in various bodily sites of decomposing corpses [12].

In a study, swabs were taken from the proximal large intestines between 9 to 20 days postmortem. Real-time quantitative PCR (RT-qPCR) was conducted using group-specific primers targeting 16SrRNA genes to detect three common gut bacteria: Bacteroidetes, Lactobacillus, and Bifidobacterium. The results showed that the relative abundance of Bacteroides and Lactobacillus species decreased significantly and exponentially ($p < 0.05$) as the postmortem interval (PMI) increased. These findings suggest that these two bacteria could potentially serve as reliable quantitative indicators for estimating the time since death in medico-legal investigations [10-12].

In a separate study, researchers identified five highly abundant species (Staphylococcus sp., Streptococcus sp., Clostridium sp., Enterococcus sp., and Escherichia sp.) and a total of 21 different bacterial genera as postmortem colonizers. The study highlighted important findings relevant to the field of thanatomicrobiome research. Firstly, it was observed that sampling of cadaver tissue samples should ideally be done within 7 days after death. Secondly, the liver and pericardial fluids were identified as optimal body sites for sampling as they remained relatively free from microbial colonization for up to 5 days postmortem.

In a related thanatomicrobiome investigation, the study examined the relative quantities of commensal gut bacteria that migrated into the liver and ascites of autopsied cirrhotic livers. The results revealed that Enterobacteriaceae were the most commonly translocated bacteria into the affected hepatocyte tissues. These findings shed light on the

dynamics of microbial translocation in diseased liver tissues and its relevance to thanatomicrobiome studies [12,13].

The diversity of bacterial communities in partially skeletonized lower rib bones from 12 corpses was investigated. The study revealed that 99.2% of the sequences belonged to six bacterial phyla: Proteobacteria, Firmicutes, Bacteroidetes, Actinobacteria, Acidobacteria, and Chloroflexi. Interestingly, these communities exhibited similarities to gut-associated bacteria. However, as the bones progressed toward the dry skeletal remains stage, the bacterial communities began to resemble those typically found in soil. Based on these findings, the authors proposed that the nutrient-poor environment of corpse bones, compared to the nutrient-rich nature of soft tissue, along with the preservation of organic nutrients provided by the bones, prevented excessive bacterial growth during the initial years of skeletonization [12,14].

In a study focusing on the bloat stage of decomposition, the sequencing data revealed an increase in Firmicutes (specifically Lactobacillaceae and Bacteroidaceae families) in the abdominal cavity. Proteobacteria was the dominant phylum observed on the skin surfaces of both the head and torso areas throughout the decomposition process. However, once the carcasses ruptured, there was a significant decrease in Firmicutes on the skin. Based on these findings, a "microbial clock" was developed, which accurately estimated the postmortem interval (PMI) within a 3-day range, corroborating the actual time of death. The microbial clock refers to the time-dependent succession of microbial diversity during the decay process, providing valuable insights into the progression of decomposition [12,15].

Few studies were also conducted to assess the time since immersion in an aquatic environment based on microbial colonization. Proteobacteria and Firmicutes were identified as major players. Their colonization and succession were predicted to be useful in real scenarios [12,16,17].

Transcriptome analysis via RNA sequencing was performed on liver tissues from 27 Italian and United States corpses spanning 3.5 hours to 37 days postmortem. Eight liver tissue-specific gene biomarkers (e.g., AMBP and AHSG) were utilized in a highly specific single-blind study, accurately identifying postmortem liver tissues from autopsy-derived organ samples. Mapping results showed that 98-100% of sequencing reads aligned to these liver biomarkers, confirming the potential use of gene expression signatures to validate tissue fragment identities up to 37 days of autolysis [18].

During the autopsy, tissue samples were obtained from the prostates of five cadavers by a medical examiner. Following RNA extraction, cDNA synthesis was performed, and the concentration of cDNA was determined. The cDNA was then subjected to apoptosis-related gene expression profiling using a human PCR Array. The results of the PCR Array demonstrated that, at 38 hours after death, a majority of the genes involved in apoptosis induction and positive regulation (such as caspases) exhibited higher expression levels compared to five days postmortem. The expression of anti-apoptotic genes, including BAG1, BCL2, and the negative regulator of apoptosis XIAP, showed a significant increase in a time-dependent manner. However, the expressions of pro-apoptotic genes such as TP53 and TNFSF10 did not exhibit significant upregulation [19].

A study investigated gene expression shutdown after death by identifying mRNA transcripts that increased in relative abundance postmortem in mice and zebrafish. A time series analysis spanning up to 96 hours postmortem revealed significant increases in the abundance of 1063 genes. The profiles of these transcripts displayed non-random patterns over time. While most transcript levels increased within 0.5 hours postmortem, some exhibited increases at 24- and 48-hour postmortem. Functional analysis of the most abundant transcripts revealed categories such as stress, immunity, inflammation, apoptosis, transport, development, epigenetic regulation, and cancer. These findings suggest a stepwise shutdown of gene expression occurs during organismal death, characterized by the apparent increase of specific transcripts with varying abundance peaks and durations [20].

One could argue that certain pathways may have evolved to promote healing or "resuscitation" after severe injury, which could confer an adaptive advantage. The observed increase in transcripts related to inflammation response, for instance, may suggest that still-functioning cells sense signals of infection or injury following the body's death. Alternatively, these increases could be attributed to the rapid decay of repressors of genes or entire pathways, resulting in gene transcription. A further detailed study is warranted to gain insights into this phenomenon, potentially informing improved preservation methods for organs intended for transplantation [20].

Postmortem transcriptional regulation is a highly complex process involving various cellular components. The degradation rates of mRNA transcripts differ across different types of postmortem tissues and their unique gene expression patterns. Although mRNA molecules can persist for extended periods, they are prone to degradation, with specific genes exhibiting half-lives ranging from minutes to weeks. Postmortem genetic studies have the potential to enhance organ transplantation techniques.

In studies focusing on postmortem gene expression in cardiac tissues, ten reference genes were identified, with cyclophilin A (CYCA) and TATA box-binding protein (TBP) displaying the most stable mRNA. Similarly, in postmortem muscle tissues, succinate dehydrogenase complex subunit A (SDHA) and TBP genes exhibited stable mRNA levels. Moreover, specific mRNA markers associated with forensic body fluid identification, such as PPBP for blood, FDCSP for saliva, MSMB for semen, and MSLN for vaginal secretions, were successfully validated through distinct expression patterns in their respective body fluids.

In a related forensic study, mRNA markers including hemoglobin alpha (HBA), matrix metalloproteinase 7 (MMP7), and matrix metalloproteinase 11 (MMP11) were explored as differentiating markers between menstrual and peripheral blood stains. These findings highlight the potential utility of mRNA markers in forensic investigations [21-24].

Brain RNA degrades linearly after death. 18S rRNA is more stable than Beta-actin mRNA in the postmortem period. Their ratio can be used to predict the Time since death.

Discussion

There are a lot of grey areas in autopsy practice in particular and the field of medicine in general. Molecular medicine

is emerging as a great lens to understand them. The forensic autopsy now truly extends from the scene to the gene. We live in exciting times.[5] It is not uncommon for an autopsy surgeon to encounter cases where there are no Anato-morphological insignia towards the cause of death. The persistent challenge of exact postmortem interval before autopsy lingers on to date. The ultimate goals of medicine are to reduce the disease burden and enhance the longevity of humanity. Replacing morbid organs/tissues with new ones seems to be a logical and practical approach being practiced the world over. With the advent of cost-effective organ transplant technologies, there is a strong need to increase the supply of donor organs to meet the long waiting list of recipients. Molecular transplant medicine is an area of research that's blossoming in biology labs.

It is very much necessary to study the postmortem expression of genes in human tissues to understand the appropriate cellular mechanisms involved in it like apoptosis, stress response, and survival strategies employed by each cell, every organ, and the body as a whole. An insight into these areas may shed new light on the area of cadaver transplant when combined with the emerging technologies in tissue engineering, and regenerative medicine/stem cell medicine for creating bio-engineered organs.

The era of histopathology for confirmation of morbid anatomy/ abnormality is coming to a close and we are inching towards more conclusive evidence in cytogenetics and molecular diagnostics. The day is not so far when we may link a few sets of thanatomarkers/biomarkers for every single mechanism of death.

However, it is always borne in mind that all these techniques will complement and strengthen the traditional autopsy and it's really difficult for any of them to emerge as a substitute for routine autopsies shortly. Human molecular genetics is a very dynamic branch with volumes of literature being cataloged every day. Interpretation of all the findings of the molecular autopsy is fraught with a lot of difficulties like hitherto unreported variants, penetrance patterns, and epigenetic influences to name a few. Hence it is always advisable to seek the opinion of a professional human molecular geneticist as and when required.

Perhaps as of now, there's no single medico-legal center in our country with a dedicated molecular autopsy program. It is advisable to start right now at least in apex centers i.e., at least in one teaching hospital in every state. Molecular techniques in sequencing, gene mining, and diagnostics should be part of the PG curriculum in Forensic Medicine in the future.

The COVID pandemic led to the opening of PCR labs in every nook and corner of the country. Before the COVID-19 era, RT-PCR was a luxury and now it has become a necessity in every teaching hospital. There's a high likelihood that one fine day all our medico-legal centers in India may be upgraded for molecular autopsy work if a situation demands. Apart from all this, the true need for molecular autopsy gets reflected in our day-to-day work if we honestly start admitting our limitations in giving a 'cause of death' to every case based on just gross pathology.

Indications for Molecular Autopsy [5]

- Sudden cardiac death (structural and non-structural heart disease) – genetic panels to assess primary arrhythmia syndromes and/or

cardiomyopathies may be helpful (Comment: if considering an unexplained dilated cardiomyopathy in a person under 30 years, also examine skeletal muscle to assess for a generalized myopathic process)

- Vascular disorders (aortopathy / arteriopathy) – connective tissue disease panels (Marfan Syndrome, Ehlers-Danlos Syndrome, Loeys-Dietz Syndrome, familial thoracic aortic aneurysm, and dissection, syndromic arthropathies) – Sudden deaths in these scenarios.
- Sudden and unexpected death in infants and young children (SIDS / SUDI, SUDC) – a subset of these cases likely involves genetic cardiovascular disease – much still unknown about the pathophysiology of the SUDI cohort.
- Sudden unexpected death in epilepsy (SUDEP) – some preliminary evidence suggests that primary arrhythmia syndromes may present as a seizure disorder. There are also familial forms of true seizure disorders.
- Other complex neurological disorders – based on clinic-pathological phenotype and family history. Some complex congenital disorders – based on clinic-pathological phenotype and family history. Thrombophilias and bleeding disorders – both disorders of platelet function and coagulopathies may have a genetic basis.
- Triad cases in infants – dependent on history, and clinical and pathological findings – may consider bleeding disorders, connective tissue disorders, or metabolic disorders.
- Deaths in the setting of positional restraint, excited delirium, unexplained death in the setting of electronic control device usage – careful consideration of primary arrhythmia syndromes or cardiomyopathies
- Sudden and unexpected death in the setting of a criminal act (i.e., homicide by heart attack) – careful consideration of primary arrhythmia syndromes or cardiomyopathies
- Other uncommon genetic syndromes identified at autopsy that may be incidentally identified at autopsy, such as autosomal dominant polycystic kidney disease, hereditary spherocytosis, connective tissue disorders, genetic cancer syndromes, etc.

Sampling Considerations

10 ml of blood in EDTA and/or 1 Cm^3 fresh Spleen and/or Liver or 2 Cm^3 Muscle or Skin should be preserved for molecular autopsy. Samples are to be transported to the laboratory as early as possible. If there is a delay, samples are to be sent frozen at -80 degrees Celsius. DNA can be directly extracted from the samples for study (Figure 1).

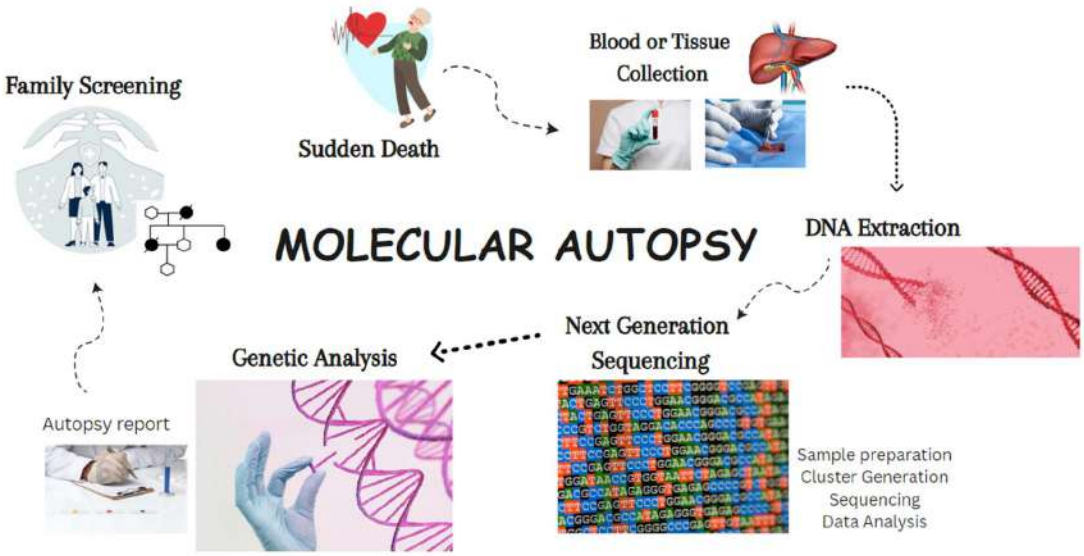


Figure 1. Workflow of Molecular Autopsy.

It is also interesting to note that micro-RNA can be extracted from even Formalin Fixed Paraffin Embedded samples also. Micro RNA is emerging as a very handy tool in forensic settings considering its stability in different settings.

The traditional method to preserve autopsy tissues in formalin for microscopic examination makes the tissues unusable for current PCR and Sanger sequencing-based molecular analysis. Non-formalin-based storage solutions, such as RNA later, should be used. Non-formalin fixatives allow rapid stabilization and protection of the cellular nucleic acids without creating damage (e.g., cross-linking) in the DNA double strands [5].

Indian Scenario

There is no dedicated molecular autopsy program anywhere in India. The problem with the present state of affairs is that few autopsy surgeons try to fit every death into some or the other diagnosis. If negative autopsy rates are reflected in the statistics, it becomes more conducive to establishing the necessity for molecular autopsy programs everywhere. The concept of bringing in the model of differential diagnosis of death during preliminary consideration of the case will solve a lot of unnecessary dogmatic reports in our field.

The niggardly pace of functioning of the criminal justice system leading to undue delay of ancillary investigations reports has created a generation of autopsy surgeons who usurped excess authority in deciding matters related to the cause of death. Moreover, we lack a proper statutory protocol for medico-legal work. Medical and Health being a state subject in our country, there are a lot of administrative impediments to easy reform.

Institutions & Laboratories in India offering Molecular Diagnostic Services

Institutions with DM programs for Medical Genetics have the wherewithal for gene diagnosis. Centre for DNA fingerprinting & Diagnostics and Centre for Cellular & Molecular Biology, Hyderabad offer a range of quality services in the field

of molecular diagnosis. The chain of laboratories of ICMR across the country, if properly equipped, can very easily offer molecular diagnostic services. However, it is always advisable for the autopsy surgeon to discuss the matter well in advance before dispatching the sample to the laboratory to ascertain the feasibility of diagnosis. It's high time we develop cross-institute collaboration channels for the field of Molecular Forensic Medicine to flourish for the benefit of society at large.

Future Directions for Research

In our setup, it is recommended to conduct research to determine the amount of DNA obtained from various tissues at different time intervals after death. This research will help establish a standard protocol for identifying the most suitable sample for DNA extraction. Whenever possible, it is advisable to perform DNA extraction within our institute to overcome the challenges associated with maintaining a cold chain, which can be particularly difficult in our country. Though it would be impractical and foolish on our part to imagine a tremendous change in outcomes of autopsy dilemmas just by introducing a molecular autopsy program, it will certainly usher many new changes in death reporting systems. With high throughput sequencing and next-generation sequencing methods turning cheaper by the day and the cost incurred in molecular diagnosis becoming more economical, we are set to see a large volume of research in the 'thantotranscriptome' genre.

- Postmortem thanatotranscriptome studies may shower a new light on mechanisms of cellular defense that can be exploited for treating diseases. For example, new anti-apoptotic pathways, and anti-stress fighting pathways may be discovered if the high volume thanatotranscriptome is totally sequenced primarily in natural deaths and later in unnatural deaths. A ***Human Thanatotranscriptome Project*** is a need of the hour which will help in archiving the data and may lead to the identification of more causes of death and specific activated genes in specific organs/bodies as a whole. Such an approach will have ramifications for both clinical medicine and forensic medicine. The human thanatotranscriptome may solve some perennial issues plaguing autopsy surgeons like the estimation of the exact time since death.
- Thanatomicrobiome profiling studies may be conducted by selecting different places across the country and in different ecosystems to develop a microbial clock for the proper estimation of time since death. This is something similar to body farms being instituted at a cellular level to study colonization and succession patterns.
- Mining for more Thanatomarkers/ biomarkers of trauma, hypoxia, inflammation, and infection from different tissues. For example, the field of biomarkers of trauma revolutionized greatly in the recent past, markers like S100 calcium-binding protein B, Neuron Specific Enolase, Glial Fibrillary Acidic Protein, Interleukin 6, LDH, Brain-Derived Neurotrophic Factor, Ferritin, Neutrophil gelatinase-associated lipocalin, Microtubule-

associated protein Tau, etc. are under consideration [25].

- Study pharmacogenomic properties of individuals in case of drug abuse-related death to decide the manner as accidental/suicidal. These tests may be carried out as an adjunct to the already existing forensic toxicology services.
- Understanding the epigenetics of postmortem transcription may unravel the role of hitherto unknown areas of the genome described as 'junk'. Activation and silencing of such genes may have some deep secrets for all of us.
- Further research in the realm of thanatoproteomics is also the need of the hour for understanding the proteome-level interactions during survival and death. These studies can have implications for regeneration and transplant medicine.

Conclusion

Molecular Forensic Medicine will add more robustness to medico-legal work and will not only bring out the real cause of death; it will also help diagnosis of genetic diseases in the next of kin of the deceased. The branch will turn out to be a perfect link with clinical branches of medicine. The autopsy surgeon will hold the key responsibility of indicating the genetic nature of findings in the case to the family members and thereby coordinate with geneticists and genetic counselors. In our professional lifetime, we will see the zenith of the rapidly revolutionizing field of Molecular Forensic Medicine. Let us wish India will also be part of this scientific development very soon. The authors also advise the community of forensic pathologists in the country to get benefited from the Department of Health Research (DHR, GoI) sponsored molecular genetics training offered at Indian Council of Medical Research organizations.

Ethics declarations

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Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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