



Editorial

The Role of Fetal Autopsy in 2025: A Cornerstone in Fetal Loss Management and Genomic Medicine

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In the landscape of perinatal care, the fetal autopsy has long stood as a sentinel of diagnostic clarity. As we stand in 2025, its role has become more relevant and multidimensional than ever before spanning clinical, ethical, genomic, and technological domains. In a healthcare world increasingly driven by data and family-centered care, the fetal autopsy remains not merely a postmortem ritual but a pillar in the management of fetal loss and a guide for future pregnancy planning.

In the evolving conversation on perinatal health, stillbirth remains one of the most persistent and least addressed global tragedies. Despite commendable progress in reducing child and maternal mortality, the story of stillbirth is one of silence, stagnation, and profound inequality.

At its core, stillbirth is defined as the birth of a fetus with no signs of life at or after 28 weeks of gestation, a threshold standardized by the World Health Organization (WHO). However, this definition varies by country, with some nations using thresholds as low as 20 or 24 weeks, contributing to inconsistent surveillance and international comparability [1].

In 2019 alone, approximately 2 million babies were stillborn, equating to 1 every 17 seconds [2]. Unlike maternal or neonatal deaths, which have seen steady declines, the annual rate of reduction in stillbirths remains under 2%, significantly lagging behind the progress in under-five and neonatal survival [2]. This slow pace exposes a glaring gap in global health priorities: stillbirth remains largely invisible in both discourse and funding strategies.

Geographic inequity further compounds this crisis. Nearly 84% of all stillbirths occur in low- and middle-income countries (LMICs), with sub-Saharan Africa and South Asia bearing the heaviest burdens [2]. Within 6 countries—India, Pakistan, Nigeria, the Democratic Republic of Congo, China, and Ethiopia—lie half of the world's stillbirths [2]. In stark contrast, high-income countries account for just 2% of global stillbirths despite constituting 9% of total live births, underlining the deep disparities in health system access and quality [2].

But stillbirth is not merely a clinical statistic: it is a deeply emotional, social, and psychological event. It strikes at the heart of parenthood and dignity, yet in many cultures remains shrouded in silence. The psychosocial aftermath

can include grief, stigma, post-traumatic stress, and long-term mental health issues. For many parents, the invisibility of their loss is intensified by the lack of acknowledgment and meaningful bereavement care [3].

One of the most troubling aspects is the chronic undercounting and misclassification of stillbirths. Inadequate civil registration, inconsistent definitions, and lack of skilled health personnel mean that many stillbirths go undocumented [4]. This data void makes it difficult for countries to target interventions or effectively track progress.

The Every Newborn Action Plan (ENAP) established a target of no more than 12 stillbirths per 1000 total births by 2030. Yet, at the current rate of decline, more than 50 countries will fail to meet this goal without significant acceleration [5]. To reverse this trend, a renewed commitment is essential—one that integrates high-quality antenatal and intrapartum care, skilled birth attendance, timely emergency obstetric services, and robust perinatal investigations.

This brings us to the critical role of perinatal autopsy and pathology. Stillbirth investigations that include fetal autopsy, placental histology, and genetic testing yield a cause of death in the majority of cases, particularly when conducted by trained professionals. Unfortunately, even in high-income settings, perinatal pathology remains under-resourced. For example, the United Kingdom, despite its strong healthcare infrastructure, reported only 64 pediatric/perinatal pathologists out of over 3000 consultants. As highlighted by Flenady and colleagues [2], perinatal pathology is fundamental to both clinical understanding and public health planning. The autopsy is not simply a retrospective act; it is a tool that informs recurrence risk counseling, family planning, and even healthcare cost containment [2], yet its utility is diminished when undervalued or excluded from postmortem protocols.

The neglect of stillbirth is, in many ways, a reflection of global gender and economic inequity. The burden falls overwhelmingly on poor women in poor countries, whose grief is often met with indifference rather than empathy. As we advance toward 2030, it is imperative that stillbirth is no longer relegated to the periphery of maternal and perinatal health strategies.

The autopsy, once the cornerstone of modern medicine, has undergone a remarkable transformation and



not always for the better. In the adult hospital setting, it has faded from routine practice into a rare, sometimes ceremonial event. Where once no hospital death was complete without an autopsy, today it is common for weeks to pass in tertiary care centers without a single postmortem examination.

The reasons are manifold: increasing confidence in clinical diagnostics, the dominance of imaging technologies, fear of litigation, limited reimbursement, and emotional discomfort in obtaining consent from grieving families. As Lloyd [6] notes in his reflection on the profession, the “decline of the clinical-pathological autopsy” is perhaps the most visible casualty of a medicine that has become increasingly technological and, paradoxically, less tactile in its final assessments.

Yet, curiously, and crucially, this decline is not universal. In fact, in 1 specific and profoundly human context, the autopsy not only survives but arguably grows in value: the realm of fetal and perinatal death.

While adult autopsies now hover near single-digit percentages in many developed health systems, perinatal autopsies have remained stable, and in some specialized centers, even increased. The reason is clear. Where adult deaths are often expected or well-documented, the death of a fetus, especially one that had passed all visible prenatal checks—remains a medical mystery and an emotional catastrophe. For families, this is often not just a loss but a catastrophe in the expected narrative of life. They seek understanding, accountability, and reassurance for the future, and that is where the perinatal autopsy still answers the call.

Fetal autopsy retains a uniquely multifaceted role in contemporary medicine. It is both diagnostic and prognostic, clinical and emotional, individual and epidemiological. It can identify congenital anomalies, confirm or challenge prenatal imaging, provide data for recurrence risk counseling, and sometimes, simply and profoundly offer a cause where none was known.

But perhaps the most significant distinction lies in motivation. In adult hospital autopsies, it is often clinicians or coroners who must justify the procedure. In contrast, fetal autopsies are frequently driven by parents themselves, grieving, bewildered, and needing answers. With compassionate support, many consent willingly, especially when the purpose is framed not as scientific scrutiny, but as a final, dignified step in their child’s story.

Moreover, fetal autopsy now exists within a broader integrated framework of prenatal diagnostics. Advances in fetal magnetic resonance imaging (MRI), postmortem micro-computed tomography (CT), chromosomal microarray, and whole-exome sequencing have all magnified the value of pathology by providing layered, correlational insight. In this model, the fetal autopsy is no longer an isolated ritual but a node in a diagnostic web involving obstetricians, radiologists, geneticists, and pathologists [2].

Public health surveillance of stillbirth, fetal anomalies, and pregnancy outcomes increasingly depends on autopsy-

informed data. Without it, national reporting risks being hollow; interventions risk being misdirected. Autopsy has become not only a tool for clinical clarity but a mechanism for accountability in maternal and perinatal care systems.

Still, it would be misleading to paint too rosy a picture. The perinatal autopsy faces its own systemic vulnerabilities. The number of trained perinatal pathologists is alarmingly low. Training pipelines are limited, and the work, technically intricate and emotionally taxing, is often undervalued.

What emerges, then, is a story of divergence. While the traditional adult autopsy struggles to maintain its place in contemporary medicine, the fetal autopsy quietly asserts its continued relevance and its necessity, even in the face of death’s deepest silence.

It is not merely an act of postmortem diagnosis, but a gesture of truth, of compassion, and of continuity for families, professionals, and public health alike.

Why Fetal Autopsy Still Matters in 2025? Despite the rise of postmortem imaging and genetic diagnostics, conventional autopsy remains the gold standard, offering unparalleled insight into fetal pathology. Hutchinson *et al.* [7] emphasize that comprehensive fetal postmortem examination yields the highest diagnostic return, particularly in unexplained intrauterine fetal death (IUFD), surpassing even advanced genomic approaches in many contexts.

Similarly, the Royal College of Obstetricians and Gynaecologists’ 2024 guidelines affirm that autopsy—especially when combined with placental histology, can yield a cause in up to three-quarters of stillbirths [8]. It is this capacity for closure, for transforming tragedy into understanding, that cements the autopsy’s irreplaceable role.

Despite its invaluable diagnostic and prognostic yield, fetal autopsy may be declined by parents for a variety of reasons, often rooted in religious, cultural, or emotional beliefs. In certain faith traditions, such as Islam and Judaism, there may be theological concerns about the integrity of the body after death, though perspectives vary and allowances are sometimes made for urgent medical reasons. Cultural taboos surrounding death and the handling of the body can also impede acceptance. Additionally, the profound grief following stillbirth can make discussions about autopsy particularly distressing, especially when not handled with sensitivity and clear communication. Studies have shown that families are more likely to consent when the procedure is explained compassionately, when minimally invasive alternatives are offered, and when the process is framed as a way to seek answers and honor the baby’s life [2,9].

The Integration of Genomics and Imaging: where autopsy once stood alone, it now cooperates with powerful allies. Genetic testing—especially whole-exome and microarray analysis—has emerged as a critical adjunct. A compelling example comes from Zhang *et al.* [10], who discovered novel compound mutations in the *DNAH11* gene via fetal autopsy in laterality disorders.

Simultaneously, technologies like micro-CT and MRI offer non-invasive or minimally invasive options. Simcock *et al.* [11] report a striking increase in autopsy consent rates following the implementation of a micro-CT program, with diagnostic yield remaining strong even in macerated cases. These methods are not replacements but complements, especially valuable where cultural or parental objections to dissection exist.

New Paradigms: From Pathology to Prediction. Autopsy today informs more than just a retrospective cause. It guides prognostic counseling, recurrence risk, and therapeutic planning. Jain stresses its critical role in formulating future pregnancy strategies in a multidisciplinary framework [12]. Likewise, Garabedian *et al.* [13] recommend autopsy as a required component of postmortem evaluation, especially in cases where genetic contributions are suspected.

In rare cases, an autopsy can also uncover unusual pathologies that may otherwise go unrecognized. For instance, Paudice *et al.* [14] described a stillbirth linked to a giant hepatic hemangioma and placental chorangiosis, emphasizing the need for comprehensive anatomical assessment in ambiguous deaths.

Ethical and Cultural Dimensions: despite its value, fetal autopsy remains underutilized. As outlined in the Global Stillbirth Advocacy Guide, families are often denied full investigation due to structural inequities, cultural discomfort, or lack of skilled personnel [3]. The role of respectful bereavement care, transparent communication, and support systems cannot be overstated.

Professional guidelines such as the Royal College of Pathologists (RCPATH) Autopsy Practice Document further reiterate that even in limited or modified autopsies, standardization and transparency remain crucial [15].

A Diagnostic and Moral Imperative: fetal autopsy is not a relic of the past but a living, evolving practice at the crossroads of modern medicine. In an age that embraces precision health, autopsy continues to bridge the known and unknown, providing clarity for clinicians, closure for families, and direction for future care.

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VGv and FB jointly conceived and designed the research study. VGv and FB critically revised the work for important intellectual content. Both authors contributed to editorial changes in the manuscript. Both authors have read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

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During the preparation of this work, the authors used ChatGPT for syntactic and grammatical purposes only, as they are not native English speakers. No generative AI tools were employed to create or modify the scientific content of the manuscript. After using this tool, the authors carefully reviewed and edited the text as needed and take full responsibility for the content of the publication.

References

- [1] World Health Organization. ICD-10: International statistical classification of diseases and related health problems. 10th edn. WHO: Geneva. 2010.
- [2] Flenady V, Sexton J. Epidemiology of Fetal and Neonatal Death. In Khong TY, Malcomson RDG (eds.) Keeling's Fetal and Neonatal Pathology. 6th edn. Springer: Berlin, Germany. 2022.
- [3] International Stillbirth Alliance. Preventing and addressing stillbirths along the continuum of care: A global advocacy and implementation guide. ISA: New Jersey. 2023.
- [4] Reinebrant HE, Leisher SH, Coory M, Henry S, Wojcieszek AM, Gardener G, *et al.* Making stillbirths visible: a systematic review of globally reported causes of stillbirth. BJOG: an International Journal of Obstetrics and Gynaecology. 2018; 125: 212–224. <https://doi.org/10.1111/1471-0528.14971>.
- [5] World Health Organization. Every newborn action plan progress report 2020. WHO: Geneva. 2020.
- [6] Lloyd RV. Pathology: Historical and contemporary aspects. 1st edn. Springer Nature: Cham. 2023.
- [7] Hutchinson JC, Potocki L, Van den Veyver IB. Current Controversies in Prenatal Diagnosis 2: Conventional Postmortem Examination Remains the Gold Standard for the Anatomical Examination of Fetal Loss. Prenatal Diagnosis. 2025. <https://doi.org/10.1002/pd.6754>. (online ahead of print)
- [8] Burden C, Merriel A, Bakhbaki D, Heazell A, Siassakos D, Royal College of Obstetricians and Gynaecologists. Care of late intrauterine fetal death and stillbirth: Green-top Guideline No. 55. BJOG: an International Journal of Obstetrics and Gynaecology. 2025; 132: e1–e41. <https://doi.org/10.1111/1471-0528.17844>.
- [9] Sauvegrain P, Carayol M, Piedvache A, Guéry E, Bucourt M, Zeitlin J. Low autopsy acceptance after stillbirth in a disadvantaged French district: a mixed methods study. BMC Pregnancy and Childbirth. 2019; 19: 117. <https://doi.org/10.1186/s12884-019-2261-3>.
- [10] Zhang S, Wang J, Sun L, Han J, Xiong X, Xiao D, *et al.* Investigation of the genetic and clinical features of laterality disorders in prenatal diagnosis: discovery of a novel compound heterozygous mutation in the DNAH11 gene. Archives of Gynecol

- cology and Obstetrics. 2024; 310: 695–704. <https://doi.org/10.1007/s00404-024-07574-3>.
- [11] Simcock IC, Arthurs OJ, Hutchinson JC, Sebire NJ, Jacques TS, Sekar T, *et al.* Impact of non-invasive post-mortem micro-CT imaging on a fetal autopsy service: a single centre retrospective study. *Clinical Radiology*. 2024; 79: 791–798. <https://doi.org/10.1016/j.crad.2024.06.015>.
 - [12] Jain V. Antepartum Fetal Demise: Toward Diagnostic and Therapeutic Efficacy of Management. *Journal of Obstetrics and Gynaecology Canada*. 2025; 47: 102799. <https://doi.org/10.1016/j.jogc.2025.102799>.
 - [13] Garabedian C, Sibiude J, Anselem O, Attie-Bittach T, Bertholdt C, Blanc J, *et al.* Fetal death: Expert consensus of the French College of Obstetricians and Gynecologists. *International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics*. 2025; 168: 999–1008. <https://doi.org/10.1002/ijgo.16079>.
 - [14] Paudice M, Peñuela LA, Torielli F, Spina B, Remorgida V, Buffelli F, *et al.* Giant Hepatic Hemangioma and Placental Chorangiosis: A Unique Case of Stillbirth? *Fetal and Pediatric Pathology*. 2019; 38: 175–181. <https://doi.org/10.1080/15513815.2018.1564159>.
 - [15] The Royal College of Pathologist. Guidelines on autopsy practice: neonatal death. 2019. Available at: <https://www.rcpath.org/static/0a7c073e-c773-4941-a1e998df666e17e3/G168-Guidelines-on-autopsy-practice-Neonatal-death.pdf> (Accessed: 5 June 2025).