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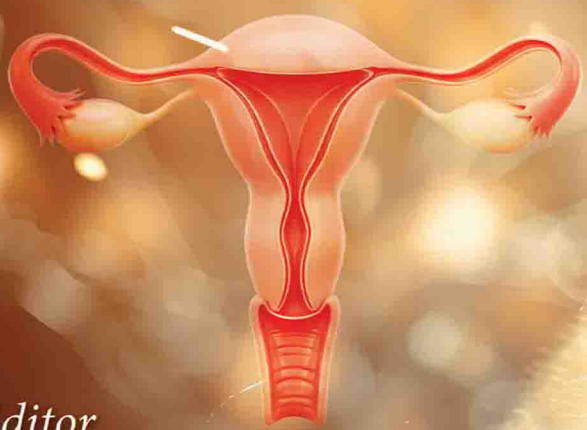
Common Medical Disorders and Recommendations in Obstetrics and Gynecology



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CHAPTER 9

Intrauterine Fetal Demise: Assessment and Future Planning

Vrunda Joshi

LEARNING OBJECTIVES

- To know the definition and epidemiology of stillbirth.
- To understand the etiology and investigation in a case of stillbirth.
- To formulate delivery plan.
- To counsel for fetal autopsy.
- To discuss bereavement care and provide appropriate counseling for future pregnancy.

Chapter Outline

- Epidemiology
- Etiology
- Pathophysiology of Intrauterine Fetal Death
- Assessment of Stillbirth
- Fetal Autopsy
- Genetic Testing
- Laboratory Studies
- Imaging
- Communicating the Diagnosis of Stillbirth
- Support Services and Bereavement Care
- Treatment/Management
- AETCOM Considerations
- Key Points
- Academic Assessment

INTRODUCTION

Intrauterine fetal death is defined as the death of fetus after 20th week of gestation and stillbirth is defined when a fetus dies inside the uterus or is delivered without signs of life after 20 weeks of gestation or weighing >350 g when gestational age is not known.[1]

In alignment with the World Health Organization, fetal death is defined as extraction of a fetus after 20 weeks of gestation that shows no signs of life such as breathing, heartbeat, or movement.

EPIDEMIOLOGY

Knowledge of stillbirth epidemiology is key to identifying vulnerable populations and improving prevention approaches.

Age[2]

Advanced maternal age:

- Increased risk of aneuploidy
- Increased risk of medical complications of pregnancy
- By 40 years of age, the estimated risk is 1 in 116 for nulliparous women and 1 in 304 for multiparous women. Lethal chromosomal abnormalities account for approximately 13% of stillbirths, with Down syndrome contributing 23%, Edwards syndrome 21%, and Patau syndrome 8%. Advanced paternal age (over 40 years) is also associated with an increased risk of stillbirth.

Race[3,4]

Racial disparities in stillbirth rates have been observed, with non-Hispanic Black women

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experiencing approximately twice the risk compared with other racial groups.

Socioeconomic Status

- Socioeconomic status is inversely related to stillbirth risk, with higher rates seen among women of lower socioeconomic standing.
- Delayed or inadequate prenatal care further increases the risk, as women who do not receive antenatal care have nearly fourfold higher odds of stillbirth compared with those who attend the recommended number of visits. Even limited attendance of one to two prenatal visits is associated with a 2.9-fold increase in stillbirth risk compared with attending four visits.[5]

Gestational Age

In otherwise low-risk pregnancies, the risk of stillbirth increases steadily after 37 weeks of gestation. The relative risk of stillbirth when pregnancy continues, compared with delivery at the same gestational age, rises from 1.29 at 37 weeks to 1.32 at 38 weeks, 1.64 at both 39 and 40 weeks, 1.94 at 41 weeks, and 1.93 at 42 weeks. These findings indicate a marked increase in stillbirth risk once pregnancy extends beyond 41 weeks.[6]

Male *sex* stillbirths are significantly higher in number.

Multiple Pregnancy

Multiple gestations are associated with a substantially higher risk of stillbirth, with the greatest risk observed in monochorionic twin pregnancies. The prevalence of stillbirth is approximately 0.52% in singleton pregnancies, 1.4% in twin pregnancies overall, and 3.5% in monochorionic twins. The risk of stillbirth increases sharply after 37–38 weeks of gestation.[7]

ETIOLOGY

Maternal Factors (Box 1)

- *Diabetes:* Diabetes in pregnancy increases the risk of stillbirth by up to fivefold, particularly with poor glycemic control. Stillbirth rates are approximately 16.1 per 1,000 births in type 1 diabetes and 22.9 per 1,000 in type 2 diabetes. Elevated prepregnancy body mass index (BMI), higher HbA1c levels, and abnormal fetal growth further increase risk, with both growth restriction and macrosomia associated with higher stillbirth rates. The peak risk occurs at 38 weeks in type 1 diabetes and 39 weeks in type 2 diabetes, with nearly one third of diabetes-related stillbirths occurring at term.[8]
- *Hypertension:* Hypertension that is present before or early in pregnancy significantly increases the likelihood of stillbirth [odds ratio (OR) 2.01], and this risk escalates with greater disease severity.[9]
- *Obesity:* Obesity, defined as a BMI over 30 kg/m^2, is an independent risk factor for stillbirth, even when accounting for diabetes, smoking, gestational diabetes, and preeclampsia. The risk of stillbirth is approximately 8 per 1,000 for women with a BMI of 30–39.9 kg/m^2 and 11 per 1,000 for those with a BMI >40 kg/m^2.[10]
- *Substance misuse:* Placental dysfunction, vasoconstriction, hypoxia, and alteration in endogenous chemicals result in growth restriction and stillbirth. Smoking tobacco increases the risk of stillbirth by 15 per 1,000 antepartum and intrapartum. Women exposed to secondary smoking also have an increase of stillbirth. For alcohol, the OR is 1.36. Illicit drugs such as opioids, methamphetamine, and cannabis also have increased OR for stillbirth.[11]

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BOX 1: Risk factor and possible etiologies.

Maternal risk factor
- Advanced maternal age
- 35–39 (11–14/1,000)
- >40 (11–21/1,000)
- Antiphospholipid syndrome
- Autoimmune disease
- Cholestasis of pregnancy (12–30/1,000)
- Chronic hypertension (6–25/1,000)
- *Diabetes:*
  - Diet controlled (6–10/1,000)
  - Insulin dependent (6–35/1,000)
- Obesity
  - BMI >30 kg/m^2 (13–18/1,000)
- Preeclampsia
  - Without severe features (9–51/1,000)
  - With severe features (12–29/1,000)
- Previous stillbirth (9–20/1,000)
- Renal disease (15–200/1,000)
- Smoking (10–15/1,000)
- Substance abuse (alcohol, coffee >3 cups/day, cocaine)
- Systemic lupus erythematosus (40–150/1,000)
- Thrombophilia (18–40/1,000)
- Thyroid disease (12–20/1,000)

Infectious etiologies (up to 19%)
Bacterial infections:
- Listeria monocytogenes
- Treponema pallidum
- Group B streptococci
- *Escherichia coli*
- *Ureaplasma urealyticum*
- *Mycoplasma hominis*

Viral infections:
- Cytomegalovirus
- Parvovirus B19
- Enteroviruses
- HSV-1, HSV-2
- Echoviruses
- HIV

Parasitic infection
- *Toxoplasma gondii*

Fetal and placental etiologies
- Alloimmunization, red cell
- Alloimmunization, platelet

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- Chromosomal/genetic abnormalities (8–13% of all stillbirths)
  - Trisomy 21 (23%)
  - Trisomy 18 (21%)
  - Trisomy 13 (8%)
  - Monosomy X (23%)
- Other (19%)
- Complications of multifetal gestation
- Congenital malformations
- Fetal growth restriction
- Fetomaternal hemorrhage (4%)
- Intrauterine asphyxia
- Placenta previa
- Placental abruption
- Placental pathology
  - Massive chorionic intervillositis
  - Chronic villitis
  - Massive perivillous fibrin deposition
- Postdates
- Preterm labor or rupture of membranes
- Umbilical cord complications (10%) (i.e., cord prolapse, vasa previa, velamentous insertion, cord entanglement)
- Uteroplacental insufficiency

Note: Parenthetical data represents estimated rate (per 1,000 births) or prevalence (percentage) when available. (BMI: body mass index; HIV: human immunodeficiency virus; HSV: herpes simplex virus)

- *Obstetrics and conditions related to pregnancy and previous adverse outcomes of pregnancy:* A prior preterm birth or a previous small-for-gestational-age infant increases the likelihood of stillbirth in a subsequent pregnancy, with the risk further elevated when both factors are present. Additionally, a history of previous stillbirth substantially raises the risk of recurrence (adjusted OR 2.68).[12]
- *Antiphospholipid syndromes (APS):* APS is linked to intrauterine death, fetal growth restriction, preeclampsia, and preterm birth. Diagnosis requires the presence of at least one clinical criterion and one laboratory

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criterion. Laboratory confirmation involves detecting anticardiolipin antibodies, anti-β2 glycoprotein I antibodies, or the lupus anticoagulant.[13]

- *Intrahepatic cholestasis:* Intrahepatic cholestasis of pregnancy is a liver disorder marked by elevated serum bile acids and pruritus, which increases the risk of fetal complications, preterm delivery, meconium-stained amniotic fluid, and stillbirth. A 2019 meta-analysis demonstrated that stillbirth risk is significantly higher when bile acid levels reach 100 μmol/L or more.[14]
- *Placental and umbilical cord abnormalities:* Placental abnormalities, such as insufficiency due to infarctions, chronic villitis, or reduced vascularization, can impair oxygen and nutrient supply, leading to fetal growth restriction and intrauterine death. Infections and inflammation, including chorioamnionitis or villitis, can also contribute to these outcomes.[15]

Placental abruption or retroplacental hematomas can cause acute hypoxia.

Vascular lesions, maternal or fetal vascular malperfusion.

Villitis of Unknown Etiology

Villitis of unknown etiology (VUE) is a destructive villous inflammatory lesion characterized by the infiltration of maternal T cells (CD8+ cytotoxic cells) into chorionic villi. Infants whose placentas have VUE are at risk for death and abnormal neurodevelopmental outcomes at the age of 2 years.

Placental abnormalities were linked to stillbirth in fetuses both with and without evidence of growth abnormality. When stillbirth occurs in the absence of growth restriction, the effect is acute and severe, including chorioamnionitis, fetal chorionic plate vascular degenerative changes, perivillous and intervillous fibrinoid deposits, and fetal vascular thrombi in the chorionic plate. When stillbirth is associated with growth restriction, the findings are velamentous cord insertion, terminal villous hyperplasia, and parenchymal infarcts. These conditions impair placental functions to varying degrees; hence, varying degrees of fetal growth and live births are directly proportional to gestational age and fetal weight.

Umbilical Cord

Abnormalities including cord entrapment, obstruction (e.g., torsions, strictures with thrombi, knots), cord prolapse, vasa previa, and compromised fetal circulation may result in stillbirth. The International Classification of Neonatal Deaths system found that approximately 19% of stillbirths are associated with umbilical cord abnormalities. While nuchal cords occur in up to 30% of births and are not significantly linked to stillbirth, the odds of stillbirth increase with multiple nuchal loops compared to single or no loops (OR 4.65). True cord knots are associated with a significantly higher risk of stillbirth.

Infectious and Autoimmune Causes

Stillbirth related to infection varies from 5 to 22%. In developed countries, infection accounts for 19% of stillbirths before 28 weeks. When an infection is the cause of stillbirth, spontaneous preterm delivery is common. The predominant bacteria cultured include *Escherichia coli* (29%), group B streptococci (GBS) (12%), *Enterococcus* species (12%), and *Listeria monocytogenes* (rarely). Nonbacterial organisms causing stillbirth include cytomegalovirus (CMV) (8%), parvovirus B19 (3%), *Treponema pallidum* (syphilis, 2%), and herpes simplex virus (2%).[16]

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Rhesus factor incompatibility if not diagnosed may present with intrauterine fetal death.

Fetal Factors

Congenital defects, defined as physical or biochemical abnormalities, occur in 1/33 pregnancies and more risk of stillbirth: 11/1,000 for bladder dystrophy; 490/1,000 for limb–body-wall complex; 10/1,000 for cleft lip and palate; 110/1,000 for amniotic band-associated limb defects; 13/1,000 for sacral agenesis; 24/1,000 for isolated spina bifida; and 30/1,000 for holoprosencephaly (data altered due to elective termination in early pregnancy).

Fetal structural malformations (FSMs) along with abnormal copy number variations (CNVs) are significantly associated with stillbirth. Specific CNVs (mutations) may contribute to stillbirth risk.

Amniotic Fluid Abnormalities

Polyhydramnios

Polyhydramnios is defined as an amniotic fluid index (AFI) of 24 cm or more or the deepest vertical pocket of fluid of 8 cm. It significantly increases the odds of stillbirth (OR 7.64). The risk of stillbirth for women with polyhydramnios increases with gestational age, with the lowest risk at 26 weeks and increased to 7 times at 37 weeks and 11 times at 40 weeks of gestation.[17]

Oligohydramnios

Oligohydramnios is defined as an AFI of ≤5 cm or a maximum vertical pocket under 2 cm. The risk for stillbirth has increased to 11.54. Hence, delivery for oligohydramnios may be indicated at 37 weeks' gestation when no other comorbidity is identified or sooner for nonreassuring fetal monitoring.[18]

PATHOPHYSIOLOGY OF INTRAUTERINE FETAL DEATH

The primary cause of stillbirth is fetal hypoxia. The fetus depends on the placenta to exchange oxygen from the mother. The partial pressure of oxygen (pO_2) in fetomaternal circulation is only a fraction of maternal pO_2. Therefore, even minor disruptions in pO_2 can cause significant compensatory mechanisms in the fetus, redistributing blood flow to the brain, heart, adrenal glands, and umbilical cord and result in fetal growth restriction. Fetal circulation adaptation occurs at 50% reduction in the placental flow. However, when the flow reduces to 25%, these compensatory mechanisms fail, causing respiratory and metabolic acidosis, widespread vasoconstriction, and reduced blood flow to all vascular regions. Depleted cardiac glycogen stores lead to impaired myocardial contractility, generalized hypotension, bradycardia, decreased cardiac output, and ultimately fetal demise.

The cause of fetal demise in maternal diabetes is fetal hyperglycemia resulting in anaerobic metabolism and lactic acidosis followed by metabolic acidosis and death.

Biomarkers such as elevated erythropoietin, glial fibrillary acidic protein, and cardiac troponin T can be used as indicators for fetal hypoxia and potential cerebral or myocardial ischemia[19] **(Table 1)**.

ASSESSMENT OF STILLBIRTH

A thorough history along with physical examination is essential for the assessment following a stillbirth.

History

- *Key maternal factors:* Age, parity, gravidity, chronic hypertension, diabetes, hypercoagulable states, autoimmune disorders, and history of cancer

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TABLE 1: Elements of a stillbirth evaluation.

Key components	*Details*	*Comments*
	Patient history, family history • Recurrent spontaneous abortions • Venous thromboembolism • Congenital anomaly or chromosomal abnormalities • Hereditary condition or syndrome • Developmental delay • Consanguinity *Maternal history* • Previous venous thromboembolism • Diabetes mellitus • Chronic hypertension • Thrombophilia • Systemic lupus erythematosus • Autoimmune disease • Epilepsy • Severe anemia • Heart disease • Tobacco, alcohol, drug, or medication use *Obstetric history* • Recurrent miscarriages • Previous child with anomaly, hereditary condition, or growth restriction • Previous gestational hypertension or preeclampsia • Previous gestational diabetes mellitus • Previous placental abruption • Previous fetal demise *Current pregnancy* • Maternal age • Gestational age at stillbirth • Medical conditions complicating pregnancy *Cholestasis* • Pregnancy weight gain and body mass index • Complications of multifetal gestation, such as twin–twin transfusion syndrome, twin reversed arterial perfusion syndrome, and discordant growth • Placental abruption • Abdominal trauma • Preterm labor or rupture of membranes • Gestational age at onset of prenatal care • Abnormalities seen on an ultrasound image • Infections or chorioamnionitis	

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Key components	*Details*	*Comments*
Fetal autopsy	If patient declines, external evaluation by a trained perinatal pathologist will be conducted. Other options include photographs, X-ray imaging, ultrasonography, magnetic resonance imaging, and sampling of tissues, such as blood or skin	Provides important information in approximately 30% of cases
Placental examination	Includes evaluation for signs of viral or bacterial infection. Discuss available tests with pathologist	Provides additional information in 30% of cases. Infection is more common in preterm stillbirth (19 vs. 2% at term)
Fetal karyotype/ microarray	Amniocentesis before delivery provides the greatest yield. Umbilical cord proximal to placenta if amniocentesis is declined	Abnormalities found in approximately 8% of cases
Maternal evaluation at time of demise	• Fetal–maternal hemorrhage screen: Kleihauer–Betke test or flow cytometry for fetal cells in maternal circulation	Routine testing for inherited thrombophilias is not recommended. Consider cases with a personal or family history of thromboembolic disease
	• Syphilis	
	• Lupus anticoagulant	
	• Anticardiolipin antibodies	
	• β2-glycoprotein antibodies	
In selected cases	Indirect Coombs	If not performed previously in pregnancy
	Glucose screening (oral glucose tolerance test, hemoglobin A1C)	In the large for gestational age baby
	Toxicology screen	In cases of placental abruption or when drug use is suspected

- *Current pregnancy factors:* Abnormal bleeding, trauma, excessive or inadequate weight gain, infections, hypertension, preeclampsia, anemia, diabetes, fetal anomalies, and fetal growth restriction
- *Obstetric history:* Previous preterm delivery, stillbirth, fetal growth restriction, and pregnancies complicated by conditions such as deep vein thrombosis, pulmonary embolism, diabetes, or need for blood transfusion
- *Infection exposure:* Maternal exposure to Zika virus, parvovirus, CMV, toxoplasmosis, syphilis, or malaria
- *Immunization history:* Documentation of relevant vaccinations
- *Family history:* Genetic disorders, recurrent pregnancy loss or stillbirth, parental age, and history of inherited conditions
- *Social history:* Employment, nutrition, substance use, domestic violence, travel, and contact with animals or pets

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- *Prenatal laboratory tests:* Complete blood count, blood type and screen, hepatitis B surface antigen, syphilis testing, human immunodeficiency virus (HIV) testing, rubella status, prenatal aneuploidy screening, diabetes screening, and urine analysis with culture

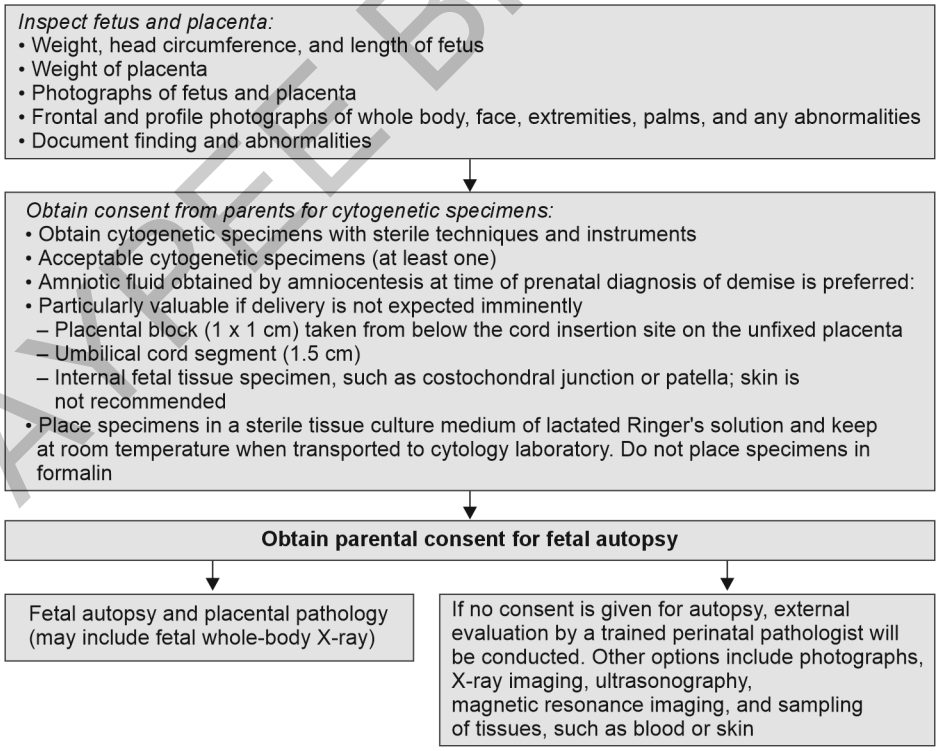
Physical Examination

- *Vital signs and infection assessment:* Evaluate maternal vital signs and check for clinical signs of infection
- *Fetal assessment*: Attempt to detect fetal heart tones using a Doppler device. If fetal heart tones cannot be confirmed, perform an abdominal ultrasound promptly to determine fetal viability.
- *Ultrasound evaluation:* Assess for congenital anomalies, fetal growth parameters, amniotic fluid volume (using the deepest vertical pocket), signs of isoimmunization, infection indicators, and multiple gestation **(Flowchart 1)**

Placental Examination

- *Gross examination:* Measure the size of the placental disc, weight (kg), and diameter (cm).
- *Structure:* Determine whether the placenta is intact and note the presence of accessory lobes.
- *Lesions:* Maternal surface: Look for calcifications, hematomas, and infarcts.
- *Fetal surface:* Identify hemangiomas.
- *Amnion:* Evaluate color and the presence of lesions such as amnion nodosa or amniotic bands.

Flowchart 1: Fetal and placental evaluation.



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- *Umbilical cord:* Examine structure, number of vessels, length (cm), coiling (normal, hypo-, or hypercoiled), knots, torsion, and insertion site (central, velamentous, marginal, or furcate).
- *Multiple gestation:* Assess chorionicity as well as amnionicity.

Consider obtaining a wedge sample of the placenta for genetic testing. The placenta should be submitted to pathology in a 1–2 L container with 100–200 mL of normal saline, accompanied by relevant maternal and fetal history. If pathological examination is delayed, the placenta can be stored at 4°C.

FETAL AUTOPSY

A thorough examination of the fetal body, both externally and internally, is conducted to identify congenital anomalies, infections, or other pathological conditions. Fetal autopsy can help find the cause of death in approximately 42.4% of cases. Key components of a complete fetal autopsy include:

- *Consent:* Obtain parental or guardian consent prior to the procedure.
- *External gross examination:* Document photographs, radiographs, body measurements, maceration, overall appearance, and obtain skin samples for cytogenetic analysis.
- *Internal gross examination:* Perform a Y-shaped incision, collect routine cultures, and examine the abdomen, thorax, and neck in situ.
- *Organ examination:* Remove the organ block and brain, dissect individual organs, weigh all organs, and document any abnormalities.
- *Brain examination:* Conduct gross and histologic evaluation after fixation.
- *Histologic analysis:* Examine tissues microscopically.
- *Documentation:* Review and record gross and histologic findings, establish a provisional anatomic diagnosis, and review ancillary studies.
- *Reporting:* Prepare a comprehensive report including final anatomic diagnosis, summary of clinical history, gross and microscopic descriptions, and clinicopathologic correlation.

GENETIC TESTING

Genetic testing can aid in establishing a diagnosis in approximately 11.9% of stillbirth cases. If fetal tissue is unavailable due to parental refusal, maceration, or poor sample quality, amniocentesis performed prior to delivery may provide necessary genetic material. The primary techniques include chromosomal microarray analysis (CMA) and karyotyping, with CMA being preferred because it can detect submicroscopic genetic abnormalities and can be performed on nonviable tissue. Exome or whole-genome sequencing may also be employed to identify causative single-nucleotide variants or small insertions and deletions.

LABORATORY STUDIES

Routine laboratory investigations in the evaluation of stillbirth include:

- *Antiphospholipid antibodies:* Detected in 11.1% of cases
- *Fetomaternal hemorrhage:* 6.4%
- *Glucose screening:* 1.6%
- *Parvovirus testing:* 0.4%
- *Syphilis screening:* 0.2%
- Assessment for disseminated intravascular coagulation (DIC)

IMAGING

Postmortem imaging techniques, including MRI, ultrasound, and computed tomography (CT), are valuable tools for evaluating stillbirth, particularly when autopsy is declined. Postmortem MRI, the most extensively studied modality, demonstrates

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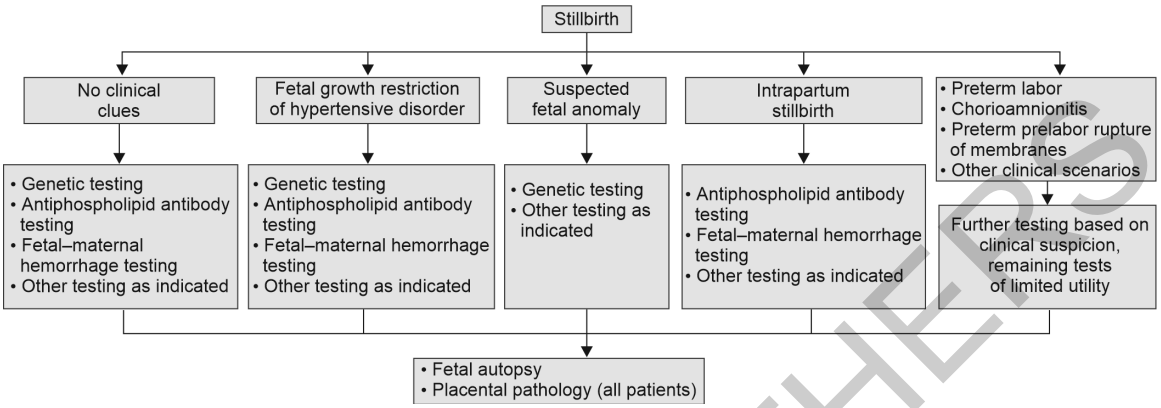
Flowchart 2: Evaluation of stillbirth based on test utility in a variety of clinical scenarios.



Source: Adapted from Page JM, Christensen-Linquest L, Thorsten V, Parker CB, Reddy UM, Dudley DJ, et al. Diagnostic test for evaluation of stillbirth: results from the stillbirth collaborative research network. Obstet Gynecol. 2017;12:699-706.

high diagnostic accuracy (77–94%). When combined with placental pathology and genetic testing, these imaging methods provide a noninvasive approach to obtain crucial diagnostic information, aiding in the determination of stillbirth causes **(Flowchart 2)**.

COMMUNICATING THE DIAGNOSIS OF STILLBIRTH

Key components include confirming the diagnosis, discussing delivery options, and addressing both the physical and the psychological needs of the patient and family. The diagnosis of stillbirth should be confirmed with a second ultrasound if needed, and patients should be offered the opportunity to view the ultrasound images if they wish.

- *Meeting emotional needs:* Patients experience shock, denial, grief, anger, and depression. Validate them and tell them that it is not their fault.
- *Emotional intelligence in care:* Offer clear explanations of the next steps.
- *Memory-making and bereavement support:* Family and especially the mother should be asked if they want to hold the baby and/or keep some memory as a lock of hair, hand, or foot impressions.
- *Counseling about autopsy:* Offer respectful information and support regarding autopsy options
- *Cultural and religious considerations:* Address and respect any cultural or religious preferences concerning the handling of the baby's remains. Offer respectful counseling about autopsy.

SUPPORT SERVICES AND BEREAVEMENT CARE (BOX 2)

Principles of bereavement care are as follows:

- Individualized
- Good communication
- Shared decision-making
- Recognition of parenthood
- Acknowledging a partner's and the family's grief
- Awareness of burials, cremation, and funerals
- Ongoing emotional and practical support
- Health professionals trained in bereavement care
- Health professionals with access to self-care

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BOX 2: Evaluation of stillbirth.

Recommended in all cases:
- Fetal postmortem examination (MRI if postmortem declined)
- Placental pathology
- Karyotype or microarray of amniocentesis or CVS prenatally, or placental biopsy after delivery
- Fetomaternal hemorrhage testing: Kleihauer–Betke or flow cytometry

Useful in some cases:
- Syphilis serology
- Indirect Coombs (if not performed earlier in pregnancy)
- Toxicology screen
- Parvovirus B19 IgM and IgG
- Lupus anticoagulant, IgG and IgM anticardiolipin, and anti-β2-glycoprotein antibodies
- Factor V Leiden, prothrombin gene mutation, antithrombin III, protein C&S levels (must be done at least 6 weeks postpartum)
- Glucose screening test
- Thyroid-stimulating hormone
- Serology/testing for other infectious etiologies (CMV, toxoplasmosis)
- Bile acids

Generally not useful
- Routine TORCH titers
- ANA testing

(ANA: antinuclear antibody; CVS: chorionic villus sampling; IgG: immunoglobulin G; IgM: immunoglobulin M)

TREATMENT/MANAGEMENT

The method and timing of delivery after a stillbirth depend on the gestational age at which the death occurred, maternal obstetric history (e.g., previous hysterotomy), and maternal preference. Although most patients desire prompt delivery, the timing of delivery is not critical; coagulopathies associated with prolonged fetal retention are uncommon.

Options for delivery of the stillborn fetus typically include induction of labor or hysterotomy/cesarean section.

Variables are gestational age and history of previous one or more number of cesarean sections.

Several methods of induction of labor have been described. A variety of routes of administration of prostaglandin analogs including prostaglandin E2 (PGE2) and PGF2α have been used with success. Use of oral mifepristone and antiprogestin in 200 and 400 mg doses given 24 hours apart followed by vaginal tab misoprostol in varying doses has been found to be the method of choice due to patient satisfaction and minimal discomfort and a comparably short onset to delivery interval. Other methods can be used as intracervical Foley catheter followed by tab misoprostol or intravenous (IV) oxytocin, or the use of tab misoprostol alone or IV oxytocin in a primed cervix.

Presence of a scarred uterus, however, demands an individualized approach which takes into consideration the gestational age, integrity of the scar, and position of the placenta in relation to the scar. Elective hysterotomy or cesarean section may be required if more than one previous section and larger gestational age or suspected morbid adhesion of placenta.

Methods of Delivery

- Cervical priming:
  - Mechanical—intracervical Foley catheter insertion
  - Pharmacological—prostaglandin analogs —gel/inserts/tablets
    - Mifepristone oral tablets
- Induction of labor
  - IV oxytocin
  - Tablet misoprostol
- Surgical
  - Hysterotomy
  - Cesarean section

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Counseling for the Risk of Stillbirth Recurrence (Management of Subsequent Pregnancies)

A preconception appointment is recommended for all women with a history of stillbirth. In this visit, records from the previous pregnancy are reviewed with a discussion of possible etiologies, to get investigations done, and to create a plan for the management of maternal medical conditions as well as to correct potentially modifiable risk factors **(Box 3; Tables 2 and 3)**.

BOX 3: Management of subsequent pregnancy after stillbirth.

Preconception or initial prenatal visit:
- Detailed medical and obstetric history
- Evaluation/workup of previous stillbirth
- Determination of recurrence risk
- Discussion of increased risk of other obstetrical complications
- Smoking, alcohol, and illicit substance cessation
- Weight loss in obese women
- Genetic counseling if family genetic condition exists
- Support and reassurance

First trimester:
- Dating ultrasound by crown-rump length
- *First-trimester screen:* PAPP-A, hCG, and nuchal translucency
- Diabetes screen
- Antiphospholipid antibodies/thrombophilia workup (only if specifically indicated)
- Support and reassurance

Second trimester:
- Fetal anatomic survey at 18–20 weeks
- *Quadruple screen:* MSAFP, hCG, estriol, and inhibin-A
- Support and reassurance

Third trimester:
- Serial ultrasounds to rule out fetal growth restriction, starting at 28 weeks
- Fetal movement counting starts at 28 weeks
- Antepartum fetal surveillance starting at 32 weeks or 1–2 weeks earlier than gestational age of the previous stillbirth if it occurred before 32 weeks
- Support and reassurance

Delivery: Elective induction at 39 weeks or before 39 weeks if desired by the couple and fetal lung maturity documented by amniocentesis

(hCG: human chorionic gonadotropin; MSAFP: maternal serum alpha-fetoprotein)

AETCOM CONSIDERATIONS

A primigravida with BMI of 30 kg/m^2 has missed her antenatal checkups after 20 weeks of gestation. She presents in routine antenatal OPD at 32 weeks. On examination, fetal heart sounds could not be auscultated. Ultrasonography and Doppler show an intrauterine fetal death.

Competencies addressed:
The student should be able to:
- Identify conflicts of interest in patient care and professional relationships and describe the correct way to communicate the diagnosis of intrauterine fetal death. Level SH
- Demonstrate empathy to patient and family with a stillbirth in a simulated environment. SH learning experience:
  - Year of study: Professional year 4
  - Hours: 5:
    - Introduction of case: 1 hour
    - Self-directed learning: 2 hours
    - Anchoring lecture: 1 hour
- Discussion and closure of case: 1 hour

KEY POINTS (TABLE 4, BOX 4)

- According to the World Health Organization, a fetal death, or "stillbirth", is defined as the delivery of a fetus after 20 weeks of gestation that shows no signs of life, including breathing, heartbeat, or movement. Possible etiology could be maternal medical conditions, fetal and placental conditions, infection, and not ascertained.
- Diagnosis by documentation of cardiac asystole on real-time ultrasound

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TABLE 2: Principles of bereavement care.

Individualized bereavement care	Bereavement care should be individualized to recognize bereaved parents' personal, cultural, or religious needs. Time needs to be spent with bereaved parents to gain an understanding of their wishes
Good communication	Communication with bereaved parents should be clear and honest. The term "your baby or babies" should be used in conversation; terms such as fetus, embryo, or spontaneous abortion should be avoided
Shared decision making	Parents should be provided with full information into any important decisions to be made regarding themselves or their baby (babies). Parents should be given adequate time to consider all options available to them
Recognition of parenthood	Recognition of parenthood and the role of memory making is vitally important as it is thought to assist with the actualization of grief and the slow transition of the parents' relationship with their baby from one of presence to one of memory. One of the greatest regrets that bereaved parents have reported is the lack of memories of their baby
Acknowledging a partner's and the family's grief	Recognition that a partner's and family's grief can be as profound as that of the mother and that their need for support should be considered and met. Support services should be made available and resources given to the parents and their families
Acknowledging that grief is individual	Recognition of the grief journey and that all bereaved parents will handle and react differently to grief. The intensity and duration of grief will be different. Health professionals should be made aware that different grief responses are normal and that there is no perfect way to grieve
Awareness of burials, cremation, and funerals	All babies, no matter what gestation, should be treated with respect at all times. Options for burial, cremation, taking baby home, home funerals, and conventional funerals should be discussed before the baby is born, if possible, to give as much time to organize, consider, and for all options to remain open. Health professionals should be aware of burial, cremation, and funeral options available in their local area
Ongoing emotional and practical support	Bereaved parents should be provided with information and referrals to both professional support and peer-to-peer support services such as First Candle. The concept of seeking support (professional or peer) should be normalized for bereaved parents and encouraged. Bereaved parents who access support services report that they feel their grief was heard, understood, and validated have greater prospects of hope for the future
Health professionals trained in bereavement care	All healthcare professionals who interact with bereaved parents should aim to attend professional development opportunities and to be familiar with the principles of bereavement care
Health professionals with access to self-care	It is OK not to be OK after the death of a baby. All staff who care for bereaved parents before, during, and after the death of a baby will be affected emotionally. Health professionals are in the "helping" profession, and when they cannot help, this can bring up difficult emotions. Staff should have good access to information about effective self-care

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- Prenatal assessment is done by a detailed history, examination, laboratory, and imaging. Investigations include detailed ultrasound, amniocentesis for microarray analysis, diabetes screening, fetomaternal hemorrhage testing, antiphospholipid antibodies, serology for parvovirus B19, CMV, and syphilis, and identifying placental pathology.
- Parental counseling includes grief management and discussion of management plan

TABLE 3: Estimated rate of stillbirth with maternal or fetal conditions.

Condition	*Estimated rate of stillbirth*[*]
All pregnancies	6.4/1,000
Diabetes	
Treated with diet (A1)	6–10/1,000
Treated with insulin	6–35/1,000
Hypertensive disorder	
Chronic hypertension	6–25/1,000
Preeclampsia	
Without severe features	9–51/1,000
With severe features	12–29/1,000
Growth-restricted fetus	10–47/1,000
Multiple gestation	
Twins	12/1,000
Triplets	34/1,000
Oligohydramnios	14/1,000
Late term pregnancy (>41 weeks)	14–40/1,000
Previous stillbirth	9–20/1,000
Decreased fetal movement	13/1,000
Systemic lupus erythematosus	40–150/1,000
Renal disease	15–200/1,000
Cholestasis of pregnancy	12–30/1,000
Advanced maternal age	
35–39 years	11–14/1,000
40 years or greater	11–21/1,000
Black maternal race	12–14/1,000
Maternal age <20 years	7–13/1,000
Assisted reproductive technology	12/1,000
Obesity (pregnancy)	
BMI ≥30 kg/m^2	13–18/1,000
Smoking >10 cigarettes per day	10–15/1,000

*Rate per 1,000 live births and stillbirths.
(BMI: body mass index)
Source: Data from Rosenstein MG, Cheng YW, Caughey AB. The mortality risk of expectant management compared with delivery stratified by gestational age and race and ethnicity. Am J Obstet Gynecol. 2014;660:e1-8.

TABLE 4: Stillbirth recommendations.

Recommendation	*Grade of recommendation*
Inherited thrombophilias have not been associated with stillbirth, and testing for them as part of a stillbirth evaluation is not recommended	1C Strong recommendation, low-quality evidence
In women who decline invasive testing, a portion of the placenta, an umbilical cord segment, or internal fetal tissue can be sent for genetic analysis	1B Strong recommendation, moderate-quality evidence
Microarray analysis, incorporated into the stillbirth workup, improves the test success rate and the detection of genetic anomalies compared with conventional karyotyping	1A Strong recommendation, high-quality evidence
Genetic evaluation for specific abnormalities should be guided by the clinical history and detected fetal abnormalities	1C Strong recommendation, low-quality evidence
Evaluation of a stillbirth should include fetal autopsy, gross and histologic examination of the placenta, umbilical cord, membranes, and genetic evaluation	1A Strong recommendation, high-quality evidence
Gross and microscopic examination of the placenta, umbilical cord, and fetal membranes by a trained pathologist is the single most useful aspect of the evaluation of stillbirth and is an essential component of the evaluation	1A Strong recommendation, high-quality evidence
The general examination of the stillborn fetus should be done promptly, noting any dysmorphic features and obtaining measurements of weight, length, and head circumference	1C Strong recommendation, low-quality evidence

Contd…

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Contd…

Recommendation	*Grade of recommendation*
Fetal autopsy should be offered because it is one of the most useful diagnostic tests in determining the cause of death	1A Strong recommendation, high-quality evidence
Genetic analyses are of sufficient yield that they should be performed in all cases of stillbirth after appropriate parental permission is obtained	1A Strong recommendation, high-quality evidence
Appropriate history and physical findings should be included in the requisition sent to the laboratory to assist the laboratory personnel to interpret cytogenetic tests	Best practice
A thorough maternal history should be taken to look for known conditions or symptoms suggestive of those that have been associated with stillbirth	Best practice
Healthcare providers should weigh the risks and benefits of each strategy in a given clinical scenario and consider available institutional expertise. Shared decision-making plays an important role in determining the optimal method for delivery in the setting of fetal demise	Best practice
The results of the autopsy, placental examination, laboratory tests, and cytogenetic studies should be communicated to the involved clinicians and to the family of the deceased infant in a timely manner	Best practice
Bereavement care should be individualized to recognize bereaved parents' personal, cultural, or religious needs	Best practice

Contd…

Contd…

Recommendation	*Grade of recommendation*
For patients with a previous stillbirth at or after 32 0/7 weeks, once or twice weekly antenatal surveillance is recommended at 32 0/7 weeks or starting at 1–2 weeks before the gestational age of the previous stillbirth. For stillbirth that occurred before 32 0/7 weeks of gestation, individualized timing of antenatal surveillance may be considered	2C Weak recommendation, low-quality evidence

BOX 4: Summary of management options.

Fetal death

Management options

Definition and epidemiology

The US National Center for Health Statistics (NCHS) defines fetal death as follows:

- "Death prior to the complete expulsion or extraction from the mother of a product of human conception, irrespective of the duration of pregnancy, and which is not an induced termination of pregnancy"
- It can be subcategorized by the gestation at which the demise occurred:
  - *Embryonic death:* ≤12^{+6} weeks
  - *Early fetal death:* 13–19^{+6} weeks
  - *Intermediate fetal death:* 20–27^{+6} weeks
  - *Late fetal death:* ≥28 weeks

Different countries may use different definitions and categorizations

Worldwide, stillbirth at ≥28 weeks' gestation complicates some 3.2 million pregnancies annually, with 98% occurring in low- and middle-income countries

Index pregnancy

Diagnosis: Documentation of cardiac asystole on real-time ultrasound

Contd…

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Contd…

Prenatal assessment

- Review history of index case for features pointing to a possible cause (pathogenesis of stillbirth is varied and can best be organized into categories of infection, maternal medical conditions, fetal and placental conditions; see **Table**)
- Counsel parents
- Grief counseling starts from the moment of diagnosis
- Explanation of what would be advised in terms of management
- Seek permission for postmortem examination; if refused then suggest MRI
- Investigations include (see also **Table**)
  - Detailed ultrasound
  - Amniocentesis or CVS for microarray
  - Diabetes screening
  - Fetomaternal hemorrhage testing
  - Antiphospholipid antibodies
  - Serology for parvovirus B19, CMV, and syphilis
  - Placental pathology

Delivery options—to be discussed with woman

- Expectant, with 80–90% of women delivering within 2 weeks of diagnosis; a coagulopathy will develop in 3–4% of women still pregnant 4–8 weeks after the fetal death
- Dilatation and evacuation (D&E) <24 weeks is safest if skilled individual is available
- The most cost-effective method of delivery is misoprostol-only induction for fetal death between 14 and 28 weeks' gestation
- Beyond 28 weeks' gestation, standard induction protocols (cervical ripening followed by oxytocin administration) are most effective

Postpartum

- Autopsy (including placenta and membranes); if declined by parents, alternatives are limited (head-sparing) autopsy, whole-body X-ray, MRI
- Placental biopsy for microarray if not performed prenatally
- Offer parents the opportunity to see, hold, and create keepsakes of their infant such as hand/footprints and photos
- Grief counseling, social services support, and referral as desired to peer support groups, religious leaders, and/or mental healthcare professionals are warranted prior to discharge from the hospital

Contd…

Contd…

Future pregnancy

Prepregnancy

- A preconception appointment is recommended for all women with a history of stillbirth to review records from that birth, discuss the possible etiologies, and create a plan to optimize any maternal medical conditions and change potentially modifiable risk factors

Prenatal

- Management should be in a specialized fetal medicine center
- Prediction of recurrence is very poor; risk factors for recurrence include maternal age and race, previous pregnancy history (in particular FGR or fetal death), maternal obesity, multiple gestations, assisted reproductive technologies (ARTs), tobacco and drug use, and other medical comorbidities such as hypertension, diabetes, antiphospholipid syndrome, and thrombophilia
- See **Box 2** for suggested regimen
- Therapy with low-dose aspirin in the patient's next pregnancy remains controversial; there is conflicting evidence of benefit in prevention of stillbirth

Labor and delivery

- Induction of labor at 39 weeks' gestation unless there is a sound clinical indication for earlier intervention
- Route of delivery to reflect findings during the current pregnancy

(CMV: cytomegalovirus; CVS: chorionic villus sampling; FGR: fetal growth restriction)

including permission for postmortem examination.

- The most cost-effective method of delivery is using oral tablet mifepristone followed by vaginal tab misoprostol. However, surgical procedures may be required in scarred uteri and placenta previa.
- Planning for future pregnancy involves consideration of recurrence.

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ACADEMIC ASSESSMENT

Multiple Choice Questions

1. **A stillbirth is defined as a fetal death after:**
   a. 28 weeks
   b. 20 weeks
   c. 24 weeks
   d. 16 weeks
2. **Which of the following is not a feature of maceration:**
   a. Skin slippage and bullae formation
   b. Reddish discoloration of skin
   c. Foul smell due to bacterial putrefaction
   d. Softening of tissues and collapse of fetal skull
3. **Diagnosis of stillbirth is by:**
   a. No perceptible fetal movement
   b. Meconium-stained liquor
   c. Unable to auscultate fetal heart sounds
   d. No cardiac pulsation on ultrasonography and Doppler
4. **Genetic and chromosomal abnormalities account for stillbirth:**
   a. 50%
   b. 02%
   c. 15%
   d. 30%

Short Answer Questions

1. **What maternal factors may contribute to the occurrence of a stillbirth?**
2. **What are the principles of bereavement care when dealing with a stillbirth?**
3. **How can you evaluate a stillborn baby?**
4. **What are the methods for induction of labor in a stillbirth pregnancy?**

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Common Medical Disorders and Recommendations in Obstetrics and Gynecology

Medical education in obstetrics and gynecology (OB-GYN) has undergone significant transformations to reach its current state, with the field adapting to advancements in technology, evolving patient needs, and a growing emphasis on multidisciplinary approaches to health care. This textbook *Common Medical Disorders and Recommendations in Obstetrics and Gynecology* has been designed with postgraduates and practicing clinicians in mind. The content has been formulated to include and cover common medical disorders including the practical challenges faced in uncommon scenarios like polytrauma, abuse survivors, substance abuse, etc. Each chapter follows a structured outline with key highlights, AETCOM elements, and self-assessment section. We are certain that comprehensive content aided by key points would empower practicing OB-GYN clinicians for accurate diagnosis and management in challenging situations.

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