25th September 2021

Stillbirth Society of India

International Stillbirth Alliance Member

Theme of the Month:

Perinatal Pathology in Stillbirth

STILLBIRTH
SOCIETY OF INDIA

www.stillbirth.org

From the Editor's Desk

Dear Readers,

We are greatly honoured to be entrusted the work of editing the e-newsletter of the Stillbirth Society of India. The theme for this month's e-newsletter is **"Study of Perinatal Pathology [Fetal and Placental] in Stillbirth".**

Perinatal death is a devastating obstetric complication. Determination of the cause of death helps in understanding the etiopathogenesis behind the catastrophic event. It is an indispensable aid to the bereaved parents yearning to understand the recurrence risk and appropriate prevention and management. We have put in dedicated efforts to compile and bring forth to you few very scholarly articles illustrating the same.

Dr. Nuzhat Aziz beautifully addresses the magnitude of the problem of stillbirths and leaves the reader enthusiastic about the plan of action needed to reduce stillbirths.

Dr. Sunil Jaiman, Chairman of the Committee for Study of Perinatal Pathology [fetal and placental] in Stillbirth has contributed highly relevant articles for the newsletter. One deals with the psychosocial impact of stillbirth on parents, an extremely relevant topic and many a time relegated to the background. Dr Jaiman has enriched the document by sharing his experience on the subject with us.

The article entitled 'Why study the placenta?' emphasises the importance of placental pathology in providing us clues to the cause of mishap. There are two articles dealing with faulty placentation of maternal vessels and placental dysfunction; the first is a detailed write up by Dr. Jaiman elaborating how placental dysfunction may be a window to future health of mothers and babies.

Another article dealing with faulty placentation is an excerpt from a poster presentation by Dr. Kashif M. The collection of images demonstrating different placental pathologies makes an interesting study.

The scholarly article by Dr. Seema Thakur and Dr. Chanchal Singh, meticulously brings together the broken pieces needed for the management of stillbirths in one document.

We, as a team, hope that the newsletter enhances your understanding of perinatal pathology and strengthens the concept that this is a significant, often preventable and sadly neglected cause of stillbirth.

We welcome your valuable suggestions and constructive feedback for the improvement of further editions of the e-newsletter.

Wishing all a pleasant reading experience!!!

Dr. Ayesha Ahmad
Associate Professor, ObGyn
Era's Lucknow Medical College and Hospital, Lucknow

Dr Apala Priyadarshini
Assistant Professor, ObGyn
All India Institute of Medical Sciences, Rae Bareli

Reducing Stillbirths: Concept Note

"What is a stillbirth?"

'Giving birth to death when you wanted life'

Dr. Nuzhat Aziz
Consultant, ObGyn
Fernandez Hospitals, Hyderabad
Founder Vice-President, Stillbirth Society of India

India has the largest number of stillbirths for any country, a sad 592,000 as the number of babies lost for the year 2015. [1] The reduction in stillbirth rate has been much lower than the maternal death or the neonatal mortality rates. The drive for reduction of the maternal mortality rates has not focussed on the parallel reduction of avoidable stillbirths. Lancet series on stillbirth in published in the year 2016, mentioned 10 countries as being responsible for 2/3 of stillbirths, 60% of neonatal deaths and 58% of maternal deaths that happen across the globe. The wide discrepancy in stillbirth rates varies from 1.3 to 45/1000 births between high income and low resource countries. The concept of unavoidable stillbirths due to congenital anomalies applies only to 7% of all causes, leaving a huge 93% with a scope to have an introspection; with a possibility of prevention. The psychological impact of a stillbirth on the life of a woman leaves an impact which remains through her life.

Definition: Stillbirth is defined as a baby birth after 28 weeks gestation without any signs of life [WHO definition for international comparisons]. [1] The stillbirth can occur in the antepartum period [during pregnancy] or in the intrapartum period [a child being alive for 9 months inside the mother's womb but dying in labour.

The causes of stillbirth in the antenatal period are different from intrapartum period. The proportion of antepartum to intrapartum deaths differs based on the quality of intrapartum care that is available. WHO says 1 in 2 stillbirths occur in intrapartum period in low resource countries.

Antepartum stillbirths: The important causes of a baby dying in the womb before labour are maternal conditions [hypertension, diabetes, etc], fetal growth restriction, birth defects, maternal infections [syphilis], placenta or cord related events and a small proportion of unexplained stillbirths. Many of these babies at risk of dying can be identified and timely intervention taken.

Intrapartum stillbirths: Intrapartum deaths are extremely rare in countries with low stillbirth rate, suggesting that improvement in intrapartum care will have a major impact on reducing the stillbirth rates. Early neonatal deaths within one week of birth also have a high proportion of deaths due to birth asphyxia. Intrapartum events are believed to be responsible for 19.2% of all the neonatal deaths in India. [2] Almost all deaths [97.8%] due to asphyxia occur in the first week of life, with 70% of them occurring within the first 24 hours of life [day 0]. [2]

Extrapolating This Information

If we improve fetal monitoring in labour

- 592,000 stillbirth per year in India
- 50% are intrapartum related [1]
- 296,000 intrapartum stillbirths PREVENTABLE

- 640,000 neonatal deaths per year
- 19.2% are intrapartum related [2]
- 122,880 neonatal deaths PREVENTABLE

If We Can Identify Fetal Growth Restriction

- 592,000 stillbirth per year in India
- 43% are fetal growth restricted [3]
- 254,560 FGR related stillbirths

Aiming for 50% as the detection rate

127,280 stillbirths PREVENTABLE

Proposed plan of action: The universally accepted target of reducing the stillbirth rate to 12/1000 by the year 2030 would require a planned approach in phases. Prioritising interventions which have been proven to have maximum impact, we have to focus on strengthening the intrapartum fetal monitoring and detection of fetal growth restriction. The proposed plan of action can aim to include

1. Stillbirth as a quality indicator on political and social fronts
2. Public awareness of stillbirths: Stillbirth Society of India
3. Stillbirth confidential enquiry : local with representation from all institutes joining with a chairperson.
4. Stillbirths data collection for specific regions with research assistants
5. Antenatal documentation training session to capture data
6. Respectful care, to allow more to deliver in health care facilities
7. Antenatal care protocol of high quality to minimize antenatal stillbirths
   a. Detection of fetal growth restriction
   b. Teaching fetal growth ultrasound
   c. Post term pregnancy, safe induction protocols

8. Risk stratification

9. Midwifery teams to take care of low risk mothers

10. Improving intrapartum care: fetal monitoring workshops

- Providing hand held dopplers and teaching auscultation of FHR
- Intelligent intermittent auscultation
- Providing CTG and learning CTG interpretation
- Assisted vaginal birth

11. Local stillbirths audit, classification: Concept of perinatal audits

The every new born action plan [ENAP] to end preventable deaths has a set stillbirth target of 12 per 1000 births or less by 2030. Global annual reduction rate [ARR] needs to more than double the present ARR of 2% to accomplish this target for reduction in stillbirth. [4] India may need to accelerate it much further to prevent the 'preventable stillbirths'.

In September, 2014, the Indian Ministry of Health and Family Welfare adopted the India New-born Action Plan, which includes a so-called single-digit stillbirth target [ie, a target to reduce stillbirth to less than ten per 1000 births] for 2030–the first national stillbirth prevention target. The plan is based on integrated interventions in antenatal care and care at birth for stillbirth prevention and new born survival, linked to an in progress roll-out of a national stillbirth monitoring scheme capturing rates and causes. A National Nodal centre at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, and the Technical Advisory Committee on Stillbirths, under the leadership of the Joint Secretary of the Indian Ministry of Health and Family Welfare, supports this plan. Ten sentinel sites were selected and evidence emerged that most stillbirths were preventable with simple interventions and proven the feasibility of stillbirth monitoring as a template for national scale-up of monitoring. [5]

Community actions, such as birth planning and transportation have been captured in health plans, will require a parallel approach; with an final aim of reduction of maternal and fetal mortality.

Promotion of health is the main aim of our work. We as healthcare policy makers, as maternity care providers should give prevention of stillbirths the importance it deserves. Stillbirth is the worst tragedy that can happen to a mother. Stillbirths are responsible for high incidence of psychological disturbances for years after the event.

References:

1. *Bernis LD, Kinney MV, Stones W, et al. Stillbirths: ending preventable deaths by 2030. The Lancet. 2016;387[10019]:703-16. Available as: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736[15]00954-X/fulltext [last accessed on 25th Sept. 2021]*

2. *Baqui AH, Darmstadt GL, Williams EK, et al. Rates, timing and causes of neonatal deaths in rural India: implications for neonatal health programmes. Bull World Health Organ. 2006 Sep;84[9]:706-13. Available as: https://pubmed.ncbi.nlm.nih.gov/17128340/ [last accessed on 25th Sept. 2021]*

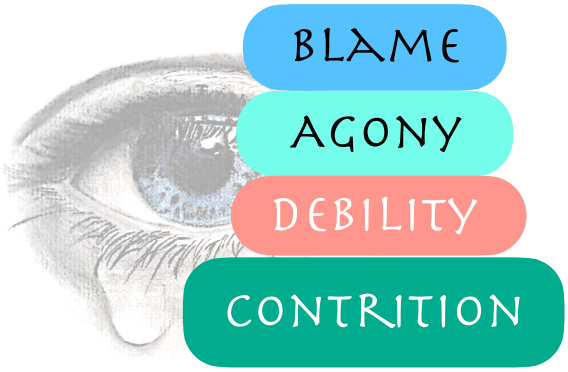
3. *Gardosi J, Kady SM, McGeown P, et al. Classification of stillbirth by relevant condition at death [ReCoDe]: population based cohort study. BMJ 2005 Nov 12;331[7525]:1113-7. Available as: https://pubmed.ncbi.nlm.nih.gov/16236774/ [last accessed on 25th Sept. 2021]*

4. *World Health Organisation. Sixty-seventh World Health Assembly. WHA67/2014/REC/1. Resolutions and decisions. WHA67.10 Newborn health action plan. Geneva: World Health Organization, 2014. Available as: https://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_JOUR6-en.pdf [last accessed on 25th Sept. 2021]*

5. *Froen JF, Friberg IK, Lawn JE et al. Stillbirths: progress and unfinished business. The Lancet,. 2016 Feb 6; 387[10018]: 574–86. Available as: https://pubmed.ncbi.nlm.nih.gov/26794077/ [last accessed on 25th Sept. 2021]*

6. *Campbell-Jackson L & Horsch A. The Psychological Impact of Stillbirth on Women: A Systematic Review. Illness, Crisis & Loss. 2014;22[3]: 237– 56. https://psycnet.apa.org/record/2014-40598-003 [last accessed on 25th Sept. 2021]*

Psychosocial Impact Of Stillbirth On Parents



Dr Sunil Jaiman
MD, DipRCPath [UK], FCAP [USA]
Section Head, Placental Pathology Perinatology Research Branch, NICHD.
Assistant Professor, Dept. Of Pathology, Hutzel Women's Hospital, Wayne State University School of Medicine, Detroit, MI, USA. Chairman Perinatal Pathology Committee, Stillbirth Society of India

I. Background

Globally, 2.7 million babies were stillborn in 2015 [1]. Rates of stillbirth vary from 2.0 per 1000 total births in Finland, 4.6 per 1000 in the United Kingdom to more than 40 per 1000 in Nigeria, Ethiopia, and Pakistan [1-4]. Despite underreporting, 98% of stillbirths occur in low and middle-income countries [LMIC], and India has the highest number of stillbirths, with an estimated 592,100 deaths per year [5]. World Health Organisation [WHO] estimated a rate of 22 stillbirths per 1000 total births [6] out of which 67% occur in rural families [2,3]. It is evident that even a modest reduction in India's stillbirth rate would translate into thousands of lives saved.

The death of a baby is the single most traumatic event in medicine. To lose a baby is to lose a piece of yourself.

-Dr. Burton Grebin

II. The Invisibility of Stillbirth

Despite increasing attention and investment for maternal, neonatal and child health, stillbirths remain invisible [4]. They are not counted in the Millennium Development Goals [MDGs], nor tracked by United Nations [UN], nor in the Global Burden of Disease metrics [4]. Furthermore, stillbirth is still not acknowledged as a serious public health issue on the global health agenda [4].

Stillbirths are invisible in many societies and on the worldwide policy agenda but are very real to families who experience a death [4]. Despite 30 years of attention to child survival interventions, [7,8] more than 20 years of attention to safe motherhood [9, 10] and increasing recent attention to survival of newborn babies [10-12] the focus worldwide has remained on survival after live birth. Stillbirths remain mostly ignored, not counting on policy, program, and investment agendas, both internationally and often also at the national level [13].

III. The Impact of Stillbirth and Miscarriage on Relationships

Stillbirth can be a devastating life event for women and their partners. Although it has been shown to cause prolonged grief that is comparable to any death of a child, the grief that results after a stillbirth or neonatal death has been described as complex and unique [14] at least in part because of a lack of acceptance or legitimization of the grieving process by society. Moreover, as the majority women conceive within a year of the loss [15], negative psychological effects of the loss may continue into subsequent pregnancies, despite the birth of a healthy child [16].

Grief of mothers

The grief of mothers might be aggravated by social stigma, blame and marginalization in regions where most deaths occur [13]. Most stillborn babies are disposed-off without any recognition or ritual, such as naming, funeral rites, or the mother holding or dressing the baby [13].

Beliefs in the mother's sins and evil spirits as causes of stillbirth are rife, and stillbirth is widely believed to be a natural selection of babies never meant to live [13]. However, the exact extent of the wider impact on families, society, government, and healthcare services remains unknown and is likely under-estimated [17].

Grief of mothers and fathers following a recent stillbirth

Most research has focused on mothers' experiences of perinatal loss itself or on the subsequent pregnancy, whereas little attention has been paid to both parents' experiences of having a child following late perinatal loss and the experience of parenting this child [18].

A study exploring mothers' and fathers' experiences of becoming a parent to a child born after a recent stillbirth, covering the period of the second pregnancy and up to two years after birth of the next baby found five superordinate themes emerging from the data [18]

1) Living with uncertainty
2) Coping with uncertainty
3) Relationship with the next child
4) The continuing grief processes
5) Identity as a parent

Overall, fathers' experiences seem to be similar to those of mothers', including high levels of anxiety and guilt during the subsequent pregnancy and after the child was born. Some differences between mothers and fathers regarding the grief process during the subsequent pregnancy and after their second child was born have been identified.

Mothers solely focused on protecting the [un]born child, whilst fathers in addition also took on the role as the main support of their partner during pregnancy. Fathers reported challenges with finding the space and lack of opportunities to grieve and it appeared that mothers and fathers also expressed their grief qualitatively differently. However, despite difficulties with bonding during pregnancy and at the time when the baby was born, parents' perceptions of their relationship with their subsequent child were positive.

IV. The Short and Long Term Psychological and Social Effects Associated With Stillbirth

Systematic reviews and meta-summaries have elucidated the following themes [17-22]:

1) Bereaved parents had significantly higher rates of psychological and emotional disorders including depression [both self-reported and clinical], general anxiety disorder, social phobia, agoraphobia, anger, negative cognitive appraisals such as a sense of failure and long-term guilt and other post-traumatic stress disorder [PTSD] symptoms, and suicidal ideation. Some parents were shown to experience strong feelings of social isolation and disconnection from their social environment [17].

2) Mental health issues, in some instances, arose decades after the loss.

3) Stillbirth led to avoidance of activities where parents may encounter babies or anything that reminded them of their own losses, creating voluntary social isolation.

4) Parental grief following stillbirth not legitimized by health professionals, family and society leading to disenfranchised grief.

5) Parents felt isolated, noting their identity as parents was not recognized by society; they were a parent, but without a child.

6) Fathers especially reported that they felt marginalized and unacknowledged as a grieving parent.

7) Parents recounted experiences suggesting that relationships with others had changed irrevocably.

8) Many parents found if hurtful when their baby was referred to as less than a person, as something replaceable and not to be remembered as part of their family.

9) Many parents indicated that mourning the death of a newborn was taboo and not culturally acceptable.

10) Stillbirth impacted relationships. For example, through different grief reactions/incongruent grieving styles. Divorce and relationship difficulties after stillbirth were frequently reported. The different grieving patterns or 'incongruent grief' of mothers and fathers were often cited as reason for these difficulties. For some couples this led to disputes, infidelity and, at times, physical violence.

11) In contrast, some couples stated that they became closer after the loss and now had a 'special unifying bond'. Some couples reported experiencing conflicting emotional reactions to sexual relationships. Women more frequently than men reported guilt and disturbing images, thoughts and feelings that interfered with sex.

12) Parents experienced external or internal pressures to prioritize or delay conception.

13) In subsequent pregnancies, some parents felt isolated and outside the boundaries of normality and experienced several emotional responses including depressive and other psychological symptoms.

14) Stillbirth impacted the wider family, including grandparents. Stillbirth had an adverse impact on siblings and complicate attachment for parents, including the surviving twin, and subsequent children. These effects appeared to be long lasting and could impact children's long-term mental and physical health.

15) Some parents reported feeling torn between managing their own grief and parenting siblings, whilst others found comfort at the time of grief from existing siblings.

16) After stillbirth some parents altered their activities as a coping strategy including seeking therapeutic isolation [needing time to themselves], increased or decreased religious activity, increased, or decreased sexual activity, and increased engagement with health promoting activities, work and social media. This continued into subsequent pregnancies.

17) Some parents felt the need to suppress outward grief, including during subsequent pregnancy. For fathers, especially those who perceived their social role as needing to provide emotional support for their partner and family, the burden of keeping feelings to themselves may lead to grief suppression, potentially increasing the risk of chronic psychological issues. Many mothers, most notably in LMICs, also often dealt with their grief privately and alone. Suppression of grief for both parents was reported to lead to relationship difficulties within the couple and the wider family unit.

18) Women reported stigmatization, rejection, and spousal abuse from their partner, family, and society. This was most notably reported in the majority of LMIC. Women were frequently blamed for the death of their babies, and some were thought to be under the spell of evil spirits or have tried to procure an abortion. There were reports of women being avoided, sent back to work immediately after giving birth, being divorced by their partner, suffering physical abuse, and even being forced out of their villages, thus leaving them destitute [23].

19) Parents reported mixed feelings regarding the decisions they made. Many parents reported conflicting emotions upon later re-evaluating the decisions they made when their baby was born.

20) Bereaved parents became hypervigilant with siblings, their subsequent children, and anxious about other people's children.

21) Chronic pain and fatigue were also shown to follow stillbirth for some parents. It was also reported that bereaved parents increased or decreased their use of health care services.

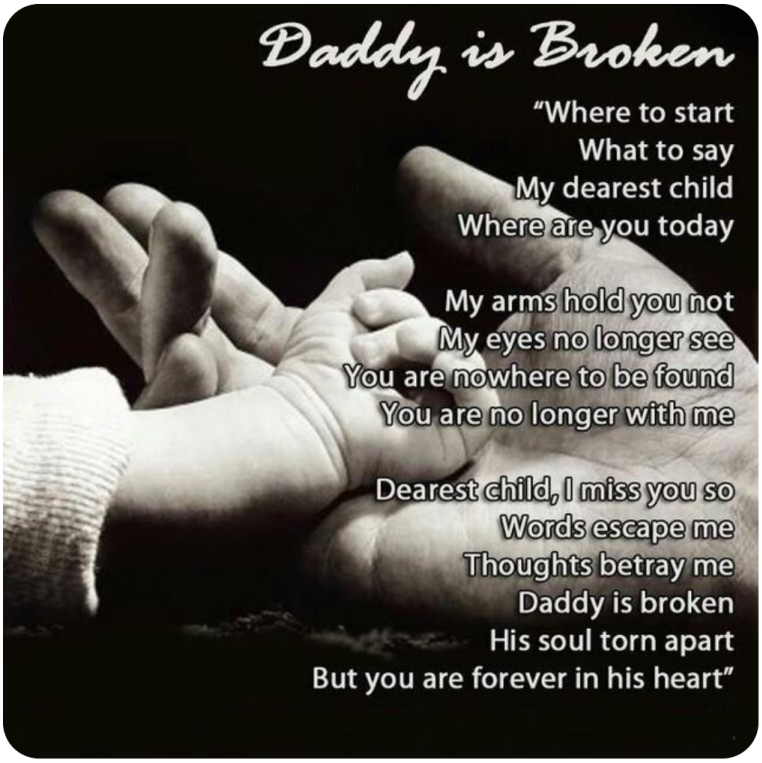
22) Employment difficulties and financial debt were reported by many.

23) Increased substance use was reported by some parents. This was another finding more commonly reported in fathers. Only one study reported increased alcohol and substance use in mothers.

24)Women developed a complex emotional response to body image. Many mothers blamed themselves for the baby's death, citing their "body's failure". Women were embarrassed and guilty of their post pregnant bodies as they did not have a baby. Conversely some women wanted to keep their bodies in a pregnant shape to stay connected to the baby.

Several women linked the grief to their body, both through physical pain and by developing an image of their body as unattractive and ugly, which also decreased sexual activity and pleasure.

25) Stillbirth changed parents' approach to life and death, self-esteem, identity, and sense of control in subsequent pregnancy, parenthood, and childrearing. As a result of stillbirth, some parents felt themselves to be more caring, thoughtful, and compassionate, less materialistic, and less likely to "take anything for granted", but several women stated that after stillbirth they did not feel "whole", that something had changed in their identity as a woman. Others reported increased or decreased fear of death after stillbirth. Many women perceived themselves as failures at the role of mother, wife, daughter, and daughter-in-law. Fathers' responses to stillbirth often corresponded with feelings of failure in the role of provider and protector.



V. Seeing and Holding Baby After Stillbirth

Several studies [21, 24-43] have suggested positive outcomes for parents who saw or held their baby. On the contrary, increased psychological morbidity was associated with current pregnancy, choice not to see their baby, lack of time with their baby and/or insufficient mementos. Three themes have been formulated 1] Positive effects of contact within a traumatic life event; 2] Importance of role of health professionals; and 3] Impact on mothers and fathers: similarities and differences [21].

Parents seeing and holding their stillborn baby have been shown to be beneficial to their future well-being [21] and there has been a proliferation of studies that challenge clinical guidelines recommending that clinicians do not encourage parental contact [21, 24-43].

VI. The Role of Healthcare Professionals in Encouraging Parents To See and Hold Their Stillborn Baby

Despite over three million recorded stillbirths, globally there are no guidelines for healthcare professionals about their role in parental contact after a stillbirth. Where clinical guidelines exist, some recommend that professionals do not encourage parental contact [22]. The guidance is based on quantitative evidence that seeing and holding the baby is not beneficial for everyone, but this concept has been challenged by bereaved parents' organizations [22].

There is no new evidence to answer the question "Should parents see and hold their stillborn baby?". Instead, studies advance the understanding of how professionals can support parents to make appropriate decisions in a novel, highly charged and dynamic situation.

1) The nature of care during labour, birth and the immediate postnatal period has long term consequences for bereaved parents' wellbeing [22]. Provision of information, guidance, and encouragement by healthcare professionals is especially welcomed by parents literally at a loss about what to do when birth brings death [22].

2) It is important for healthcare professionals to acknowledge that a baby born stillborn is still a baby, irrespective of gestation or condition [22].

3) The actual and imagined appearance of a stillborn baby varies; Parents and professionals describe beautiful and perfect babies, damaged and/or deteriorating babies, which give rise to visualizations of monsters and imagined specters until a baby is actually seen [22].

4) The time immediately after birth is the only opportunity parents will ever have to cuddle, kiss, talk-to, put a nappy on, bathe, dress, or sleep alongside their child [22].

5) Parents can regret missed opportunities and wish they had more time [22]. Memories and tokens of remembrance act as a tangible link to the baby who parents can no longer see. Tokens provide proof of existence and parenthood. Staff guidance in this area is necessary as many parents will not realize that they are able to carry out such activities, or comprehend the significance of mementos at the time [22]

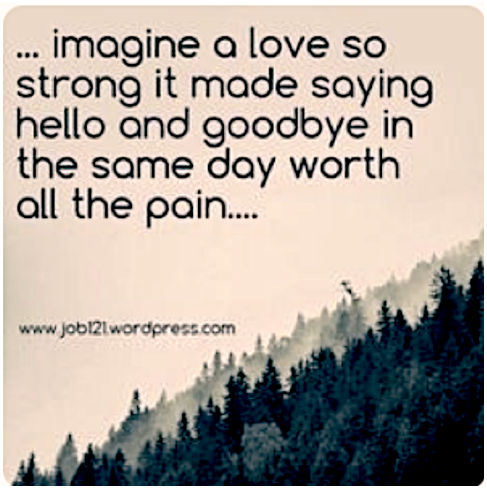
Parental contact with their stillborn baby is an emotive issue. More specific guidelines are required in their recommendations regarding parental contact. The role of healthcare professionals in encouraging parents to see and hold their stillborn baby is paramount in the short timeframe surrounding birth.

Where parents' express an initial preference not to see their baby, apprehension, or uncertainty about holding their baby, this decision should be revisited in the hours after birth. The opportunity for contact is fleeting and final [22]

VII. Conclusions

Experiencing the birth of a stillborn child is a life-changing event. The focus of the consequences may vary with parent gender and country. Stillbirth can have devastating psychological, physical, and social costs [17]. Parents who experience the tragedy of stillbirth can develop resilience and new life-skills and capacities [17].

Moreover, it is important to tailor support systems not only according to mothers' but also to fathers' needs. Difficulties experienced in bonding with the subsequent child during pregnancy and once the child is born need to be normalized [18]. Seeing and holding the baby after stillbirth has been shown to fetch a positive outcomes for parents [21]. Country specific guidelines for healthcare professionals about their role in parental contact after a stillbirth are required urgently. One therapeutic task can be to facilitate parents to create a psychic space where they can bring to life, psychically, their lost and never- really-known stillborn baby, and to let him or her to be part of the on-going family narrative [19]. Future research is required focusing on developing interventions that may reduce the psychosocial cost of stillbirth [17].



References

1.Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet [London, England]. 2016;387[10018]:587-603.
2.Oestergaard MZ, Inoue M, Yoshida S, Mahanani WR, Gore FM, Cousens S, et al. Neonatal mortality levels for 193 countries in 2009 with trends since 1990: a systematic analysis of progress, projections, and priorities. PLoS medicine. 2011;8[8]:e1001080.
3.Zupan J. Perinatal mortality in developing countries. The New England journal of medicine. 2005;352[20]:2047-8.
4.Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? Lancet [London, England]. 2011;377[9775]:1448-63.
5.Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet Global health. 2016;4[2]:e98-e108.
6.Altijani N, Carson C, Choudhury SS, Rani A, Sarma UC, Knight M, et al. Stillbirth among women in nine states in India: rate and risk factors in study of 886,505 women from the annual health survey. BMJ open. 2018;8[11]:e022583.
7.Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet [London, England]. 2003;361[9376]:2226-34.
8.Rohde J, Cousens S, Chopra M, Tangcharoensathien V, Black R, Bhutta ZA, et al. 30 years after Alma-Ata: has primary health care worked in countries? Lancet [London, England]. 2008;372[9642]:950-61.
9.Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why. Lancet [London, England]. 2006;368[9542]:1189-200.
10.Rosenfield A, Maine D. Maternal mortality--a neglected tragedy. Where is the M in MCH? Lancet [London, England]. 1985;2[8446]:83-5.
11.Knippenberg R, Lawn JE, Darmstadt GL, Begkoyian G, Fogstad H, Walelign N, et al. Systematic scaling up of neonatal care in countries. Lancet [London, England]. 2005;365[9464]:1087-98.
12.Shiffman J. Issue attention in global health: the case of newborn survival. Lancet [London, England]. 2010;375[9730]:2045-9.
13.Froen JF, Friberg IK, Lawn JE, Bhutta ZA, Pattinson RC, Allanson ER, et al. Stillbirths: progress and unfinished business. Lancet [London, England]. 2016;387[10018]:574-86.
14.DeFrain J, Martens, L., Stork, J., Stork, W. The psychological effects of a stillbirth on surviving family members. Omega-Journal of Death and Dying. 1991;22:81–108.
15.Hughes PM, Turton P, Evans CD. Stillbirth as risk factor for depression and anxiety in the subsequent pregnancy: cohort study. BMJ [Clinical research ed]. 1999;318[7200]:1721-4.
16.Blackmore ER, Côté-Arsenault D, Tang W, Glover V, Evans J, Golding J, et al. Previous prenatal loss as a predictor of perinatal depression and anxiety. The British journal of psychiatry : the journal of mental science. 2011;198[5]:373-8.
17.Burden C, Bradley S, Storey C, Ellis A, Heazell AE, Downe S, et al. From grief, guilt pain and stigma to hope and pride - a systematic review and meta-analysis of mixed-method research of the psychosocial impact of stillbirth. BMC pregnancy and childbirth. 2016;16:9.
18.Campbell-Jackson L, Bezance J, Horsch A. "A renewed sense of purpose": mothers' and fathers' experience of having a child following a recent stillbirth. BMC pregnancy and childbirth. 2014;14:423.
19.Cena L, Lazzaroni S, Stefana A. The psychological effects of stillbirth on parents: A qualitative evidence synthesis of psychoanalytic literature. Zeitschrift fur Psychosomatische Medizin und Psychotherapie. 2021;67[3]:329-50.
20.Cena L, Stefana A. Psychoanalytic Perspectives on the Psychological Effects of Stillbirth on Parents: A Protocol for Systematic Review and Qualitative Synthesis. Front Psychol. 2020;11:1216.
21.Kingdon C, Givens JL, O'Donnell E, Turner M. Seeing and Holding Baby: Systematic Review of Clinical Management and Parental Outcomes After Stillbirth. Birth [Berkeley, Calif]. 2015;42[3]:206-18.
22.Kingdon C, O'Donnell E, Givens J, Turner M. The Role of Healthcare Professionals in Encouraging Parents to See and Hold Their Stillborn Baby: A Meta-Synthesis of Qualitative Studies. PLoS One. 2015;10[7]:e0130059.
23.Sisay MM, Yirgu R, Gobezayehu AG, Sibley LM. A qualitative study of attitudes and values surrounding stillbirth and neonatal mortality among grandmothers, mothers, and unmarried girls in rural Amhara and Oromiya regions, Ethiopia: unheard souls in the backyard. Journal of midwifery & women's health. 2014;59 Suppl 1:S110-7.
24.Cacciatore J. Effects of support groups on post traumatic stress responses in women experiencing stillbirth. Omega. 2007;55[1]:71-90.
25.Cacciatore J. The unique experiences of women and their families after the death of a baby. Social work in health care. 2010;49[2]:134-48.
26.Cacciatore J, Bushfield S. Stillbirth: the mother's experience and implications for improving care. Journal of social work in end-of-life & palliative care. 2007;3[3]:59-79.
27.Cacciatore J, Erlandsson K, Rådestad I. Fatherhood and suffering: a qualitative exploration of Swedish men's experiences of care after the death of a baby. International journal of nursing studies. 2013;50[5]:664-70.
28.Cacciatore J, Rådestad I, Frederik Frøen J. Effects of contact with stillborn babies on maternal anxiety and depression. Birth [Berkeley, Calif]. 2008;35[4]:313-20.
29.Downe S, Schmidt E, Kingdon C, Heazell AE. Bereaved parents' experience of stillbirth in UK hospitals: a qualitative interview study. BMJ open. 2013;3[2].
30.Erlandsson K, Warland J, Cacciatore J, Rådestad I. Seeing and holding a stillborn baby: mothers' feelings in relation to how their babies were presented to them after birth--findings from an online questionnaire. Midwifery. 2013;29[3]:246-50.

31.Lasker JN, Toedter LJ. Satisfaction with hospital care and interventions after pregnancy loss. Death studies. 1994;18[1]:41-64.
32.Lathrop A, Vandevusse L. Affirming motherhood: validation and invalidation in women's perinatal hospice narratives. Birth [Berkeley, Calif]. 2011;38[3]:256-65.
33.Lovell A. Some questions of identity: late miscarriage, stillbirth and perinatal loss. Social science & medicine [1982]. 1983;17[11]:755-61.
34.Rådestad I, Nordin C, Steineck G, Sjögren B. Stillbirth is no longer managed as a nonevent: a nationwide study in Sweden. Birth [Berkeley, Calif]. 1996;23[4]:209-15.
35.Rådestad I, Steineck G, Nordin C, Sjögren B. Psychological complications after stillbirth--influence of memories and immediate management: population based study. BMJ [Clinical research ed]. 1996;312[7045]:1505-8.
36.Rådestad I, Surkan PJ, Steineck G, Cnattingius S, Onelöv E, Dickman PW. Long-term outcomes for mothers who have or have not held their stillborn baby. Midwifery. 2009;25[4]:422-9.
37.Säflund K, Sjögren B, Wredling R. The role of caregivers after a stillbirth: views and experiences of parents. Birth [Berkeley, Calif]. 2004;31[2]:132-7.
38.Samuelsson M, Rådestad I, Segesten K. A waste of life: fathers' experience of losing a child before birth. Birth [Berkeley, Calif]. 2001;28[2]:124-30.
39.Surkan PJ, Rådestad I, Cnattingius S, Steineck G, Dickman PW. Events after stillbirth in relation to maternal depressive symptoms: a brief report. Birth [Berkeley, Calif]. 2008;35[2]:153-7.
40.Trulsson O, Rådestad I. The silent child--mothers' experiences before, during, and after stillbirth. Birth [Berkeley, Calif]. 2004;31[3]:189-95.
41.Turton P, Evans C, Hughes P. Long-term psychosocial sequelae of stillbirth: phase II of a nested case-control cohort study. Archives of women's mental health. 2009;12[1]:35-41.
42.Worth NJ. Becoming a father to a stillborn child. Clinical nursing research. 1997;6[1]:71-89.
43.Yamazaki A. Living with stillborn babies as family members: Japanese women who experienced intrauterine fetal death after 28 weeks gestation. Health care for women international. 2010;31[10]:921-37.

"Grief changes shape, but it never ends."

-Keanu Reeves [Father of a stillborn baby]

Management of Stillbirth: Joining the Broken Pieces

Dr. Seema Thakur
MS [ObGyn], DM [Medical Genetics] Senior Consultant, Fortis Hospital and Birthright, Madhukar Rainbow Children's Hospital, Delhi. Member, Perinatal Pathology Committee, Stillbirth Society of India

Dr Chanchal Singh
MD [ObGyn], MRCOG, FICOG, Fellowship Maternal Fetal Medicine [NUH], Fetal Medicine Foundation [UK]. Lead Consultant, Fetal Medicine, Birthright, Madhukar Rainbow Children's Hospital, Delhi. Chairman, FGR Committee, Stillbirth Society of India

Introduction

Still birth or IUD [intrauterine death] is common. Still birth or fetal death is defined as fetal deaths at 20 weeks or greater of gestation [if the gestational age is known], or a weight greater than or equal to 350 g if the gestational age is not known. As per estimated birth prevalence by WHO, India has highest number of still births worldwide with estimated birth prevalence of 25/1000 live births. [2.5%].

Fetal death/still birth is one of the most difficult situations an obstetrician would face in her practice. For parents this is devastating. The two basic questions for the clinician and the patients are - What was the cause of death in this pregnancy and Will this happen again. The management of still birth is all about knowing the cause, risk factors and association and how to prevent in next pregnancy.

Causes of still birth include maternal, fetal, and placental causes. Fetal causes would include structural anomaly, chromosomal anomaly or monogenic or epigenic causes. In this article we review comprehensive evaluation of fetus, placenta and cord along with genetic testing to detect fetal and placental causes behind still birth. Evaluation of a fetal and placental causes of stillbirth should include:

- Fetal autopsy
- Gross and histo-pathologic examination of placenta, umbilical cord, membranes
- Genetic testing

I. Examination of Fetus

Fetal autopsy should be offered because it is one of the most useful diagnostic tests in determining the cause of death if the parents give consent. If families decline autopsy s partial autopsy, gross examination by a trained geneticist, ultrasonography, and especially magnetic resonance imaging are particularly useful. Fetus is examined externally as well as internally by incision.

External Examination [Fig 1]:

External examination consists of measurements and documentation of any external malformations, dysmorphic facies and X-ray.

Clinical Photography: It should be performed in all cases of perinatal post-mortem examination. Standard full body frontal and side view of face in all cases with selected additional close ups for specific abnormalities in dysmorphic babies with macroscopic abnormalities.

Figure 1: Intrauterine death at 35 weeks, showing meconium stained lips and tongue

Evaluation of gestational age, any dysmorphism, external anomaly and measurements: Body weight, crown-rump length, crown-heel length, foot length, head circumference.

Skeletal Survey:

- X-ray is recommended for suspected skeletal dysplasia, multiple malformations and unexplained stillbirth, and in particular clinical settings such as suspected fetal growth restriction.
- Skeletal survey is often performed in conjunction with post-mortem, and may detect abnormalities [mainly skeletal] which may not be detected on an external examination.

Internal Examination:

The skin incision should be midline and inverted Y- shaped or I-shaped and a systematic examination should be performed including:

Brain: Scalp, skull, cerebral hemispheres, cerebellum, midbrain, pons, medulla, thymus, corpus callosum

Neck and thorax: Thymus, Thyroid

Respiratory system: Epiglottis, larynx, trachea and main bronchi, diaphragm, left and right lung, any pleural effusions.

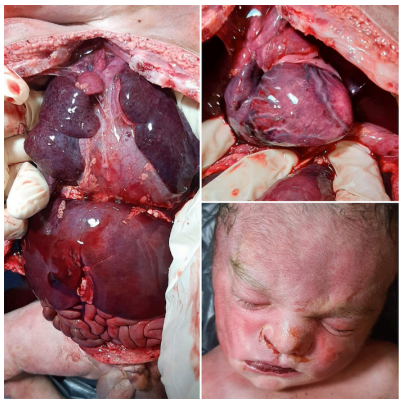


Figure 2: Intrauterine death at 35 weeks, showing dark , congested lungs and heart due to hypoxia

Cardiovascular System: Pericardial effusion, situs, axis of heart, right and left ventricle and outflow tracts, pulmonary artery and aorta.

Gastrointestinal System: Stomach, liver, spleen, Small and large intestine

Genitourinary System: Kidneys, Adrenals, Internal sex organs, Urinary bladder.

II.Examination of the Placenta and Cord

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 still- birth. [Fig 3]. This examination is for looking for abruption, umbilical cord thrombosis, velamentous cord insertion, and vasa previa. In twin pregnancy, chorionicity should be checked and vascular anastomosis can be documented in MCDA twins.

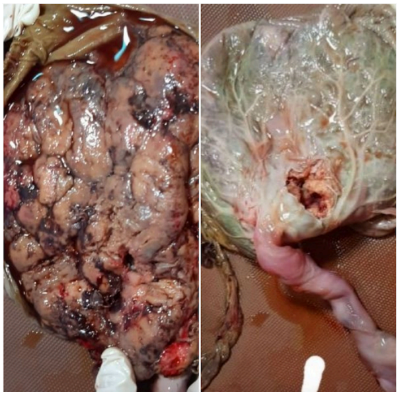


Figure 3: Gross examination of placenta and fetal membranes

Umbilical cord knots or entanglement should be noted. Length of the cord and coiling index should be measured in every case. Cord entanglement occurs in approximately 25% of normal pregnancies and most true knots are found after live births. Hence this finding should be interpreted with caution. The minimal histologic criteria for considering a diagnosis of cord accident should include vascular ectasia and thrombosis in the umbilical cord, chorionic plate, and stem villi. A regional distribution of avascular villi or villi showing stromal karyorrhexis is also suggestive of cord accidents.

III. Fetal Genetic Testing

Genetic evaluation techniques such as karyotyping, FISH, Chromosomal microarray [CMA], Exome sequencing by Next generation sequencing [NGS] have been reported in fetal sample analysis. Genetic testing by means of karyotyping has been standard practice in stillbirth, being included in the work-up for decades. As compared with karyotype analysis, microarray analysis provided a relative increase in the diagnosis of genetic abnormalities. The two largest series included were multicenter North American studies and these demonstrated a 2% [Reddy et al.] and 5% [Rosenfeld et al.] incremental yield of CMA over karyotyping for cases with pCNVs. The test success rate achieved by CMA can be as high as 90%.

CMA has many advantages as compared to karyotyping- maternal cell contamination exclusion, detection of uniparental disomy- which makes microarray suitable as the first tier test for the evaluation of stillbirths. Exome sequencing can be done if recurrent stillbirth or history of consanguinity. This will exclude monogenic disorders causing stillbirth.

How To Transport for Fetal Autopsy and Genetic Testing

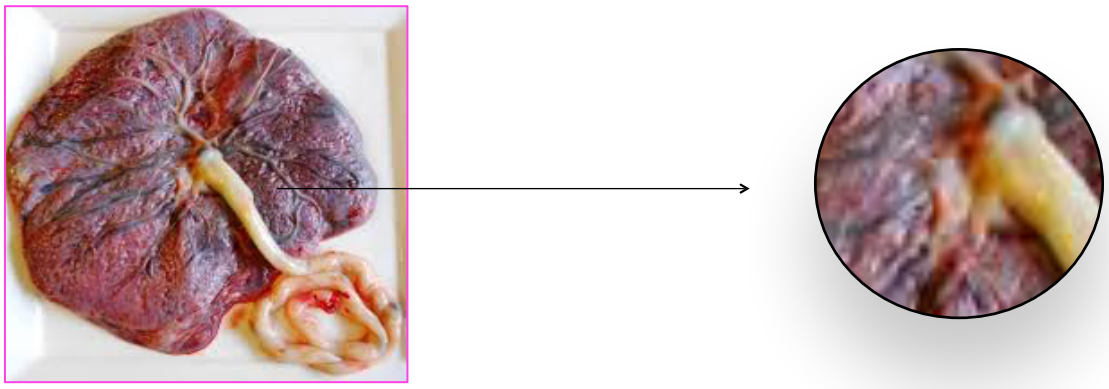
Ideally fetus and placenta should be transported in sterile normal saline, preferably in a ice box if the referral lab is located within the city.

If the fetus has to be transported to a lab outside the city- Fetus should be preserved in 10% formalin. Samples for genetic testing should be collected before putting formalin in placenta. Fig 4a and 4b shows how to collect fetal samples.

Figure 4a: Collection of POC sample

< 12 weeks	> 12 weeks
◉ Samples taken before suction, by dilatation and curettage. ◉ In medium/ sterile NS ◉ Add a drop of gentamycin [50ug/ml] & heparin	◉ Cord blood in heparin /EDTA vaccutainer ◉ Placenta, ,Fetal skin- in media or sterile NS ◉ Add a drop of gentamycin [50ug/ml] & heparin

Figure 4b: Collection of placental sample



Sample should be collected from the point where cord joins placental tissue

Conclusions

Post-mortem examination of a baby following fetal death/still birth may provide a complete or partial explanation of the pregnancy loss. Fetal autopsy and Placenta histopathology and genetic investigations may help in etiological diagnosis in about 50% cases. Autopsy is the single most useful investigation and provides information that changes or significantly adds to the clinical diagnosis in nearly half of cases. The autopsy is also a valuable audit of clinical care and may facilitate learning from adverse events

Suggested Readings

ACOG/SMFM. Obstetric Care Consensus #10: Management of Stillbirth. Am J Obstet Gynecol 2020

Why Study the Placenta?

Dr Sunil Jaiman
MD, DipRCPath [UK], FCAP [USA]
Section Head, Placental Pathology Perinatology Research Branch, NICHD.
Assistant Professor, Dept. Of Pathology, Hutzel Women's Hospital, Wayne State University School of Medicine, Detroit, MI, USA, Chairman Perinatal Pathology Committee, Stillbirth Society of India

The Importance of Placenta in the Evaluation of Stillbirth

Introduction

Approximately 2.6 million fetal deaths >28 weeks of gestation occur worldwide [1]. Pregnancy complications are associated with fetal death, such as maternal hypertension [2-8], diabetes mellitus [2,9,10], intrauterine infection [11-13] or inflammation [14-16] and placental abruption [2,6,17-21]. However, the conundrum of fetal death becomes more complicated by the fact that 25% to 62% of all stillbirths remain non-attributable to known maternal, placental, or fetal risk factors [22-28]. Substandard care contributes to 20–30% of all stillbirths and the contribution is even higher for late gestation intrapartum feta deaths [29]. However, stillbirths are not inevitable. There are many reasons to believe that further reduction in stillbirths is possible given the fact a low proportion of stillbirths have been attributed to congenital abnormality [29].

Moreover, although the below mentioned reasons have been associated with stillbirths, amelioration can substantially bring down stillbirth rates: 1] Socioeconomic disparities; 2] Suboptimum uptake of interventions; 3] Substandard patient care and 4] High proportions of stillbirths being labeled as unexplained [29].

The quality of data on stillbirth is poor and has been identified as a factor hindering progress in reducing the occurrence of stillbirth [29-32]. The strategies suggested to reduce fetal death include 1] Parental access to high-quality investigation into the causes of stillbirth, including autopsy and placental histopathology, by a skilled perinatal pathologist; 2] The need for a consensus on a classification system for stillbirth specifically addressing the contribution of placental pathology; and 3] The development of a standard that defines procedures in reporting stillbirths [29].

Why Study the Placenta?

The ease of obtaining consent to examine the placenta prompted the American College of Obstetricians and Gynecologists Committee on Genetics to emphasize that placental examination should become a routine clinical tool in stillbirth evaluation [33, 34]. The committee recommended gross and microscopic examination of the placenta, including the membranes and umbilical cord, to corroborate postmortem findings or to explain apparent fetal abnormality in stillbirth [33]. Placental pathology in stillbirth is now deemed as a clinical and research priority [29, 34, 35].

Studies from different countries have shown that the most frequent causes of fetal death are attributable to the placenta and umbilical cord abnormalities [36-57]. Similarly, the Stillbirth Collaborative Research Network reported that the most useful diagnostic test for evaluation of stillbirth has been placental pathology [56, 58]. In stillbirths associated with infection in a diverse US cohort, the most useful tests found were placental pathology and fetal autopsy with pertinent positive results in 89% and 55% cases respectively [59].

Another study compared seven classification systems for cause of death and reported that the leading cause of death was attributable to placental pathology [61]. A recent study [60] conducted to determine the association of placental pathology with the occurrence and severity of bronchopulmonary dysplasia and neonatal death in preterm infants found that neonates <29 weeks gestational age with multiple placental pathologic lesions have an increased risk for developing BPD. This suggests an interaction between placental inflammation and vascular pathology and the pathogenesis of bronchopulmonary dysplasia [60]. Another study explored the relative utility of genetic testing in contrast to placental pathology in explaining causation of death in the structurally normal stillborn population and reaffirmed the utility of placental examination in the investigation of stillbirth. The authors concluded that in cases of non-dysmorphic stillbirth where placental pathology is not able explain the cause of stillbirth, microarray analysis of fetal DNA can add further diagnostic information in only 3% of cases but can add further diagnostic confusion [61]. These findings illustrate the vital role of the placenta in determining optimal fetal development. Moreover, recognition that placental dysfunction contributes to stillbirth [38, 42, 44, 46, 53, 58, 62-67] has enhanced the focus of research in the evaluation of placental disorders as the cause of fetal death.

Placental pathology in stillbirth has been reported in previous publications [36, 42, 43, 46, 49-51, 56, 58, 64-66, 68-94]. Fetal death has been characterized by significantly higher median values for maternal age, maternal pre-pregnancy body mass index, mean arterial blood pressure, maternal obesity, tobacco use, alcohol use, drug abuse, history of preterm birth, induction of labor, and birthweight <75th percentile and downward percentiles [1, 29, 30, 56, 64, 65, 95-110]. In addition, parvovirus B19 infection and CMV infection during pregnancy have been reported to result in adverse reproductive outcome [45, 52, 56, 64, 83, 86, 95, 110-124].

Classification of Placental Pathologic Lesions Observed in Stillbirths

Placental lesions can be broadly classified as: 1] acute placental inflammatory lesions; 2] chronic placental inflammatory lesions; 3] maternal vascular malperfusion lesions; 4] fetal vascular malperfusion lesions; 5] disorders of villous maturation; 6] miscellaneous placental lesions [56, 125, 126].

Histologic Lesions of Placenta

Acute Inflammatory Lesions

Maternal inflammatory response
- Stage 1: Early acute subchorionitis or chorionitis
- Stage 2: Acute chorioamnionitis
- Stage 3: Necrotising chorioamnionitis
- Severe: Stage 3 and/or grade 2

Fetal inflammatory response
- Stage 1: Chorionic vasculitis or umbilical phlebitis
- Stage 2: Umbilical arteritis
- Stage 3: Necrotising funisitis
- Severe: Stage 3 and/or grade 2

Chronic Inflammatory Lesions

Chronic deciduitis
- Lymphocytic [without plasma cells]
- Lymphoplasmacytic

Villitis of unknown etiology [VUE]
- Low grade lesions
- High grade lesions

Chronic histocytic Intervillositis

Villitis of infectious origin

Eosionophilic T-cell vasculitis

Chronic chorioamnionitis
- Grade 1/ stage 1; Grade 1/ stage 2
- Grade 2/ stage 1; Grade 2/ stage 2

Maternal Vascular Malperfusion

Villous Changes
- ✦Villous infarct[s]
- ✦Increased syncytial knots
- ✦Villous agglutination
- ✦Increased intervillous fibrin deposition
- ✦Distal villous hypoplasia

Vascular Lesions
- ✦Persistent muscularisation of basal plate arteries
- ✦Mural hypertrophy of decidual arterioles
- ✦Acute atherosis of basal plate arteries and/or decidual arterioles
- ✦Spiral artery fibrinoid necrosis
- ✦Decidual vascular thrombosis
- ✦Persistence of endovascular trophoblast
- ✦Retroplacental haemorrhage
- ✦≥2 lesions of maternal vascular malperfusion
- ✦≥3 lesions of maternal vascular malperfusion

Disorders of villous maturation

- ✦Delayed villous maturation
- ✦Maturation arrest
- ✦Accelerated villous maturation

Fetal Vascular Malperfusion

Villous Changes
- ✦Villous stomal-vascular karyorrhexis
- ✦Hyalinised avascular villi, small foci
- ✦Hyalinised avascular villi, variable sized foci
- ✦Fetal thrombotic vasculopathy

Vascular Lesions
- ✦Thrombi in large fetal vessels
- ✦Intimal fibrin deposition, large fetal vessels
- ✦≥2 lesions of fetal vascular malperfusion

Miscellaneous lesions [hypoxic histologic patterns of placental injury]

- ✦Nucleated red blood cells
- ✦Hypercapillarised villi
- ✦Intravillous haemorrhage
- ✦Massive Perivillous fibrinoid deposition
- ✦Laminar necrosis of decidua capsular
- ✦Infections [CMV, Parvovirus]

Pitfalls of Placental Examination in Stillbirth

Stored placentas [either formalin storage/refrigeration] after 72 hours have been reported to show significant 1] reduction in the number of blood vessels per villus; 2] increase in appearances consistent with distal villous hypoplasia and 3] an increase in avascular villi [127]. Pertinently, there are no significant changes in the frequency of infarction, excessive syncytial knots, or villous immaturity [127]. This important observation implies that placental lesions of maternal vascular malperfusion [infarction, increased syncytial knots] and delayed villous maturation are not artifacts secondary to fetal death but in the eyes of inexperienced and neophyte pathologists, the artifacts secondary to fetal death may be misinterpreted as fetal vascular malperfusion lesions [56, 57].

The study by Garrod et al raises important concern that morphologic changes in the placenta should reflect pathologies and not artefacts induced by the duration of placental storage—specifically, lesions described after fetal death, such as fetal vascular malperfusion [52, 127] which can mimic post-mortem changes secondary to cessation of the fetal circulation [40, 128].

Massive perivillous fibrinoid deposition is often confused with chorionic villous infarction and vice-versa, important cause for discrepant diagnosis [129]. It is pertinent to mention that considerable variability in the definition of villous maturity [130-133]. The assessment of the presence of delayed villous maturation in the placenta is subjective, with poor concordance among pathologists and prone to much inter-observer variability [40,134]. However, the diagnosis of delayed villous maturation can be based on CD15 staining, a diagnostic marker of persistent villous immaturity and chronic placental dysfunction, which enhances an objective interpretation of this disorder of villous maturation [40, 55-57, 135-137].

Pathological pregnancies suffering from chronic hypoxia and asphyxia demonstrate an endothelial immunophenotypic transformation with significant elevation in immature CD15+ endothelial cells in the macro- [chorionic plate and stem villous vessels] and micro-vasculature [terminal villous vessels] [40, 135].

Similarly, subjective differences in the application of diagnostic criteria for accelerated villous maturation hinder reproducibility. It is known that the distinction between accelerated villous maturation and distal villous hypoplasia, both associated with maternal vascular malperfusion, needs clarification and that the pattern of accelerated villous maturation is not uniform, thus making reproducibility a challenge [125, 130, 138, 139].

Immature intermediate villi may cause considerable difficulty in diagnosing histologic differentiation of villous edema. This complexity is evident because the reticular stromal core of immature intermediate villi has a weak affinity for conventional stains, given the lack of collagen, and may impart a histologic picture of seemingly edematous villi with accumulated interstitial fluid [140].

Conclusion

Fetal death may have a systemic fetal cause, such as sepsis or hemolysis [78]; however, pulmonary, cardiac, gastrointestinal, hepatic, and renal lesions [including malformations], however striking, are rarely the primary cause of fetal death, given that the placenta facilitates respiration, nutrition, excretion, and detoxification [141]. Studies have shown that nearly 92% of the placentas from antenatal fetal death show pathologic findings [56]; therefore, placental pathologic examination associated with clinical information is essential for understanding fetal death.

References

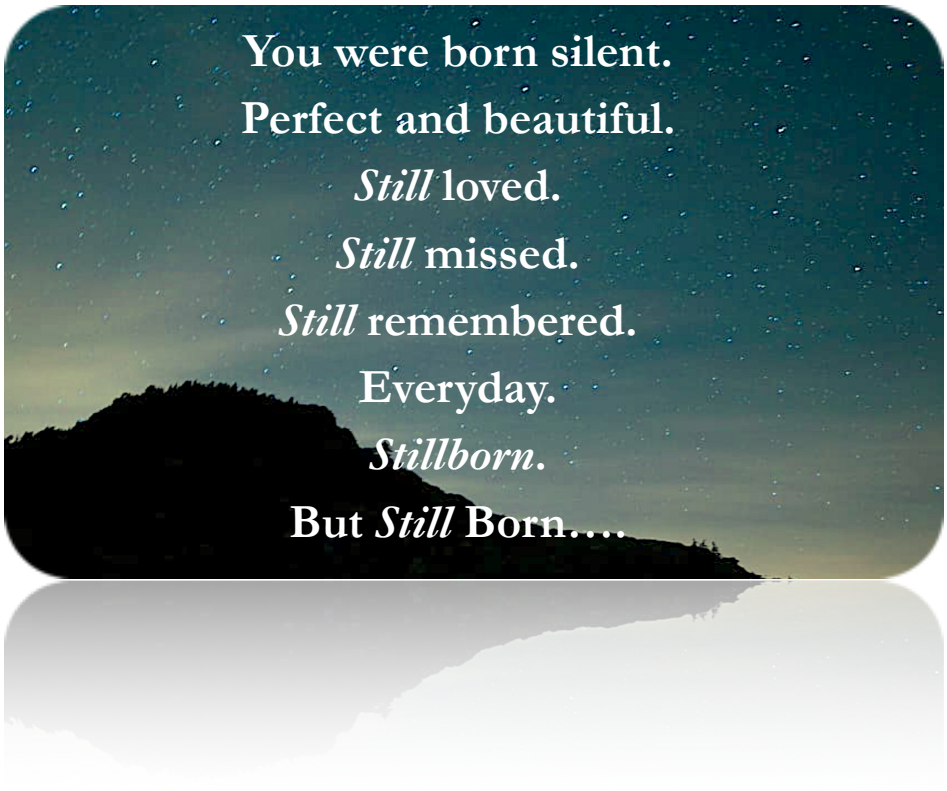
1. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet Global health. 2016;4[2]:e98-e108.
2. Smulian JC, Ananth CV, Vintzileos AM, Scorza WE, Knuppel RA. Fetal deaths in the United States. Influence of high-risk conditions and implications for management. Obstetrics and gynecology. 2002;100[6]:1183-9.
3. Allen VM, Joseph K, Murphy KE, Magee LA, Ohlsson A. The effect of hypertensive disorders in pregnancy on small for gestational age and stillbirth: a population based study. BMC pregnancy and childbirth. 2004;4[1]:17.
4. Aagaard-Tillery KM, Holmgren C, Lacoursiere DY, Houssain S, Bloebaum L, Satterfield R, et al. Factors associated with nonanomalous stillbirths: the Utah Stillbirth Database 1992-2002. American journal of obstetrics and gynecology. 2006;194[3]:849-54.
5. Ahmad AS, Samuelsen SO. Hypertensive disorders in pregnancy and fetal death at different gestational lengths: a population study of 2 121 371 pregnancies. BJOG : an international journal of obstetrics and gynaecology. 2012;119[12]:1521-8.
6. Stormdal Bring H, Hulthen Varli IA, Kublickas M, Papadogiannakis N, Pettersson K. Causes of stillbirth at different gestational ages in singleton pregnancies. Acta obstetricia et gynecologica Scandinavica. 2014;93[1]:86-92.
7. Harmon QE, Huang L, Umbach DM, Klungsoyr K, Engel SM, Magnus P, et al. Risk of fetal death with preeclampsia. Obstetrics and gynecology. 2015;125[3]:628-35.
8. Panaitescu AM, Syngelaki A, Prodan N, Akolekar R, Nicolaides KH. Chronic hypertension and adverse pregnancy outcome: a cohort study. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2017;50[2]:228-35.
9. Rosenstein MG, Cheng YW, Snowden JM, Nicholson JM, Doss AE, Caughey AB. The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes. American journal of obstetrics and gynecology. 2012;206[4]:309 e1-7.
10. Starikov R, Dudley D, Reddy UM. Stillbirth in the pregnancy complicated by diabetes. Current diabetes reports. 2015;15[3]:11.
11. McClure EM, Goldenberg RL. Infection and stillbirth. Seminars in fetal & neonatal medicine. 2009;14[4]:182-9.
12. Goldenberg RL, McClure EM, Saleem S, Reddy UM. Infection-related stillbirths. Lancet. 2010;375[9724]:1482-90.
13. Wijs LA, de Graaff EC, Leemaqz S, Dekker G. Causes of stillbirth in a socioeconomically disadvantaged urban Australian population - a comprehensive analysis. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2017;30[23]:2851-7.
14. Blackwell S, Romero R, Chaiworapongsa T, Refuerzo J, Gervasi MT, Yoshimatsu J, et al. Unexplained fetal death is associated with changes in the adaptive limb of the maternal immune response consistent with prior antigenic exposure. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2003;14[4]:241-6.
15. Blackwell S, Romero R, Chaiworapongsa T, Kim YM, Bujold E, Espinoza J, et al. Maternal and fetal inflammatory responses in unexplained fetal death. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2003;14[3]:151-7.
16. Lee J, Romero R, Dong Z, Xu Y, Qureshi F, Jacques S, et al. Unexplained fetal death has a biological signature of maternal anti-fetal rejection: chronic chorioamnionitis and alloimmune anti-human leucocyte antigen antibodies. Histopathology. 2011;59[5]:928-38.
17. Ananth CV, Berkowitz GS, Savitz DA, Lapinski RH. Placental abruption and adverse perinatal outcomes. Jama. 1999;282[17]:1646-51.
18. Ananth CV, Wilcox AJ. Placental abruption and perinatal mortality in the United States. American journal of epidemiology. 2001;153[4]:332-7.
19. Raisanen S, Gissler M, Nielsen HS, Kramer MR, Williams MA, Heinonen S. Social disparity affects the incidence of placental abruption among multiparous but not nulliparous women: a register-based analysis of 1,162,126 singleton births. European journal of obstetrics, gynecology, and reproductive biology. 2013;171[2]:246-51.
20. Stanek J. Placental examination in nonmacerated stillbirth versus neonatal mortality. Journal of perinatal medicine. 2017.
21. Nkwabong E, Tiomela Goula G. Placenta abruption surface and perinatal outcome. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2017;30[12]:1456-9.
22. Yudkin PL, Wood L, Redman CW. Risk of unexplained stillbirth at different gestational ages. Lancet. 1987;1[8543]:1192-4.
23. Cnattingius S, Haglund B, Kramer MS. Differences in late fetal death rates in association with determinants of small for gestational age fetuses: population based cohort study. BMJ [Clinical research ed]. 1998;316[7143]:1483-7.
24. Huang DY, Usher RH, Kramer MS, Yang H, Morin L, Fretts RC. Determinants of unexplained antepartum fetal deaths. Obstetrics and gynecology. 2000;95[2]:215-21.
25. Froen JF, Arnestad M, Frey K, Vege A, Saugstad OD, Stray-Pedersen B. Risk factors for sudden intrauterine unexplained death: epidemiologic characteristics of singleton cases in Oslo, Norway, 1986-1995. American journal of obstetrics and gynecology. 2001;184[4]:694-702.
26. Nappi L, Trezza F, Bufo P, Riezzo I, Turillazzi E, Borghi C, et al. Classification of stillbirths is an ongoing dilemma. Journal of perinatal medicine. 2016;44[7]:837-43.
27. Kunjachen Maducolil M, Abid H, Lobo RM, Chughtai AQ, Afzal AM, Saleh HAH, et al. Risk factors and classification of stillbirth in a Middle Eastern population: a retrospective study. Journal of perinatal medicine. 2017.
28. Basu MN, Johnsen IBG, Wehberg S, Sorensen RG, Barington T, Norgard BM. Causes of death among full term stillbirths and early neonatal deaths in the Region of Southern Denmark. Journal of perinatal medicine. 2018;46[2]:197-202.
29. Flenady V, Wojcieszek AM, Middleton P, Ellwood D, Erwich JJ, Coory M, et al. Stillbirths: recall to action in high-income countries. Lancet [London, England]. 2016;387[10019]:691-702.
30. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet [London, England]. 2016;387[10018]:587-603.
31. Froen JF, Friberg IK, Lawn JE, Bhutta ZA, Pattinson RC, Allanson ER, et al. Stillbirths: progress and unfinished business. Lancet [London, England]. 2016;387[10018]:574-86.
32. Heazell AE, Siassakos D, Blencowe H, Burden C, Bhutta ZA, Cacciatore J, et al. Stillbirths: economic and psychosocial consequences. Lancet [London, England]. 2016;387[10018]:604-16.
33. ACOG Committee Opinion No. 383: Evaluation of stillbirths and neonatal deaths. Obstet Gynecol. 2007;110[4]:963-6.
34. Pinar H, Koch MA, Hawkins H, Heim-Hall J, Shehata B, Thorsten VR, et al. The Stillbirth Collaborative Research Network [SCRN] placental and umbilical cord examination protocol. American journal of perinatology. 2011;28[10]:781-92.
35. Flenady V, Middleton P, Smith GC, Duke W, Erwich JJ, Khong TY, et al. Stillbirths: the way forward in high-income countries. Lancet [London, England]. 2011;377[9778]:1703-17.

36.Jones F, Thibon P, Guyot M, Molin A, Jeanne-Pasquier C, Guillois B, et al. Practice of pathological examinations in stillbirths: A 10-year retrospective study. Journal of gynecology obstetrics and human reproduction. 2017;46[1]:61-7.
37.Korteweg FJ, Erwich JJ, Timmer A, van der Meer J, Ravise JM, Veeger NJ, et al. Evaluation of 1025 fetal deaths: proposed diagnostic workup. American journal of obstetrics and gynecology. 2012;206[1]:53.e1-.e12.
38.Causes of death among stillbirths. Jama. 2011;306[22]:2459-68.
39.Man J, Hutchinson JC, Ashworth M, Judge-Kronis L, Levine S, Sebire NJ. Stillbirth and intrauterine fetal death: role of routine histological organ sampling to determine cause of death. Ultrasound Obstet Gynecol. 2016;48[5]:596-601.
40.Pacora P RRJS, Erez O, Bhatti G, Panaitescu B, Benshalom-Tirosh N, Jung E, Hsu C-D, Hassa S, Yeo L, Kadar N. Mechanisms of death in structurally normal stillbirths. J Peinat Med [In Press]. 2018.
41.Ptacek I, Sebire NJ, Man JA, Brownbill P, Heazell AEP. Systematic review of placental pathology reported in association with stillbirth. Placenta. 2014;35[8]:552-62.
42.Kidron D, Bernheim J, Aviram R. Placental findings contributing to fetal death, a study of 120 stillbirths between 23 and 40 weeks gestation. Placenta. 2009;30[8]:700-4.
43.Ogunyemi D, Jackson U, Buyske S, Risk A. Clinical and pathologic correlates of stillbirths in a single institution. Acta obstetricia et gynecologica Scandinavica. 1998;77[7]:722-8.
44.Tellefsen CH, Vogt C. How important is placental examination in cases of perinatal deaths? Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2011;14[2]:99-104.
45.Cnattingius S, Stephansson O. The epidemiology of stillbirth. Seminars in perinatology. 2002;26[1]:25-30.
46.Korteweg FJ, Erwich JJ, Holm JP, Ravise JM, van der Meer J, Veeger NJ, et al. Diverse placental pathologies as the main causes of fetal death. Obstet Gynecol. 2009;114[4]:809-17.
47.FJ K. Fetal death: classification and diagnostic work-up. University of Groningen/UMCG research database. 2010.
48.Korteweg FJ, Gordijn SJ, Timmer A, Erwich JJ, Bergman KA, Bouman K, et al. The Tulip classification of perinatal mortality: introduction and multidisciplinary inter-rater agreement. Bjog. 2006;113[4]:393-401.
49.Korteweg FJ, Gordijn SJ, Timmer A, Holm JP, Ravise JM, Erwich JJ. A placental cause of intra-uterine fetal death depends on the perinatal mortality classification system used. Placenta. 2008;29[1]:71-80.
50.Rayburn W, Sander C, Barr M, Jr., Rygiel R. The stillborn fetus: placental histologic examination in determining a cause. Obstet Gynecol. 1985;65[5]:637-41.
51.Horn LC, Langner A, Stiehl P, Wittekind C, Faber R. Identification of the causes of intrauterine death during 310 consecutive autopsies. European journal of obstetrics, gynecology, and reproductive biology. 2004;113[2]:134-8.
52.Parast MM, Crum CP, Boyd TK. Placental histologic criteria for umbilical blood flow restriction in unexplained stillbirth. Human pathology. 2008;39[6]:948-53.
53.Heazell AE, Martindale EA. Can post-mortem examination of the placenta help determine the cause of stillbirth? Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2009;29[3]:225-8.
54.Incerpi MH, Miller DA, Samadi R, Settlage RH, Goodwin TM. Stillbirth evaluation: what tests are needed? American journal of obstetrics and gynecology. 1998;178[6]:1121-5.
55.Seidmann L, Kamyshanskiy Y, Martin SZ, Fruth A, Roth W. Immaturity for gestational age of microvasculature and placental barrier in term placentas with high weight. European journal of obstetrics, gynecology, and reproductive biology. 2017;215:134-40.
56.Jaiman S, Romero R, Pacora P, Jung E, Bhatti G, Yeo L, et al. Disorders of placental villous maturation in fetal death. Journal of perinatal medicine. 2020.
57.Pacora P, Romero R, Jaiman S, Erez O, Bhatti G, Panaitescu B, et al. Mechanisms of death in structurally normal stillbirths. Journal of perinatal medicine. 2019;47[2]:222-40.
58.Page JM, Christiansen-Lindquist L, Thorsten V, Parker CB, Reddy UM, Dudley DJ, et al. Diagnostic Tests for Evaluation of Stillbirth: Results From the Stillbirth Collaborative Research Network. Obstet Gynecol. 2017;129[4]:699-706.
59.Page JM, Bardsley T, Thorsten V, Allshouse AA, Varner MW, Debbink MP, et al. Stillbirth Associated With Infection in a Diverse U.S. Cohort. Obstet Gynecol. 2019;134[6]:1187-96.
60.Mir IN, Chalak LF, Brown LS, Johnson-Welch S, Heyne R, Rosenfeld CR, et al. Impact of multiple placental pathologies on neonatal death, bronchopulmonary dysplasia, and neurodevelopmental impairment in preterm infants. Pediatric research. 2019.
61.Campbell J, Armstrong K, Palaniappan N, Maher E, Glancy M, Porteous M, et al. In a Genomic Era, Placental Pathology Still Holds the Key in the Nondysmorphic Stillbirth. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2018;21[3]:308-18.
62.Miller ES, Minturn L, Linn R, Weese-Mayer DE, Ernst LM. Stillbirth evaluation: a stepwise assessment of placental pathology and autopsy. American journal of obstetrics and gynecology. 2016;214[1]:115.e1-6.
63.VanderWielen B, Zaleski C, Cold C, McPherson E. Wisconsin stillbirth services program: a multifocal approach to stillbirth analysis. American journal of medical genetics Part A. 2011;155a[5]:1073-80.
64.Mecacci F, Serena C, Avagliano L, Cozzolino M, Baroni E, Rambaldi MP, et al. Stillbirths at Term: Case Control Study of Risk Factors, Growth Status and Placental Histology. PLoS One. 2016;11[12]:e0166514.
65.Gibbins KJ, Pinar H, Reddy UM, Saade GR, Goldenberg RL, Dudley DJ, et al. Findings in Stillbirths Associated with Placental Disease. American journal of perinatology. 2019.
66.Walsh CA, Vallerie AM, Baxi LV. Etiology of stillbirth at term: a 10-year cohort study. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2008;21[7]:493-501.
67.Many A, Elad R, Yaron Y, Eldor A, Lessing JB, Kupferminc MJ. Third-trimester unexplained intrauterine fetal death is associated with inherited thrombophilia. Obstet Gynecol. 2002;99[5 Pt 1]:684-7.
68.Amir H, Weintraub A, Aricha-Tamir B, Apel-Sarid L, Holcberg G, Sheiner E. A piece in the puzzle of intrauterine fetal death: pathological findings in placentas from term and preterm intrauterine fetal death pregnancies. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2009;22[9]:759-64.
69.Bukowski R, Hansen NI, Pinar H, Willinger M, Reddy UM, Parker CB, et al. Altered fetal growth, placental abnormalities, and stillbirth. PLoS One. 2017;12[8]:e0182874.
70.Man J, Hutchinson JC, Heazell AE, Ashworth M, Jeffrey I, Sebire NJ. Stillbirth and intrauterine fetal death: role of routine histopathological placental findings to determine cause of death. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2016;48[5]:579-84

71. Manocha A, Ravikumar G, Crasta J. Placenta in intrauterine fetal demise [IUFD]: a comprehensive study from a tertiary care hospital. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2018:1-9.
72. Gibbins KJ, Silver RM, Pinar H, Reddy UM, Parker CB, Thorsten V, et al. Stillbirth, hypertensive disorders of pregnancy, and placental pathology. Placenta. 2016;43:61-8.
73. Pinar H, Goldenberg RL, Koch MA, Heim-Hall J, Hawkins HK, Shehata B, et al. Placental findings in singleton stillbirths. Obstet Gynecol. 2014;123[2 Pt 1]:325-36.
74. Helgadottir LB, Turowski G, Skjeldestad FE, Jacobsen AF, Sandset PM, Roald B, et al. Classification of stillbirths and risk factors by cause of death--a case-control study. Acta obstetricia et gynecologica Scandinavica. 2013;92[3]:325-33.
75. Bukowski R CM, Conway D, Coustan D, Dudley DJ, Goldenberg RL, Hogue CJ, Koch MA, Parker CB, Pinar H, Reddy UM, Saade GR, Silver RM, Stoll BJ, Varner MW, Willinger M. Causes of death among stillbirths. Jama. 2011;306[22]:2459-68.
76. Bonetti LR, Ferrari P, Trani N, Maccio L, Laura S, Giuliana S, et al. The role of fetal autopsy and placental examination in the causes of fetal death: a retrospective study of 132 cases of stillbirths. Arch Gynecol Obstet. 2011;283[2]:231-41.
77. Chang KT, Keating S, Costa S, Machin G, Kingdom J, Shannon P. Third-trimester stillbirths: correlative neuropathology and placental pathology. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2011;14[5]:345-52.
78. Stallmach T, Hebisch G, Meier K, Dudenhausen JW, Vogel M. Rescue by birth: defective placental maturation and late fetal mortality. Obstet Gynecol. 2001;97[4]:505-9.
79. Hayati AR, Khong TY, Zainul R. The usefulness of limited placental sampling in stillbirths. The Malaysian journal of pathology. 1998;20[2]:99-102.
80. Hovatta O, Lipasti A, Rapola J, Karjalainen O. Causes of stillbirth: a clinicopathological study of 243 patients. British journal of obstetrics and gynaecology. 1983;90[8]:691-6.
81. Bar J, Schreiber L, Ben-Haroush A, Ahmed H, Golan A, Kovo M. The placental vascular component in early and late intrauterine fetal death. Thrombosis research. 2012;130[6]:901-5.
82. Ernst LM, Minturn L, Huang MH, Curry E, Su EJ. Gross patterns of umbilical cord coiling: correlations with placental histology and stillbirth. Placenta. 2013;34[7]:583-8.
83. Iwasenko JM, Howard J, Arbuckle S, Graf N, Hall B, Craig ME, et al. Human cytomegalovirus infection is detected frequently in stillbirths and is associated with fetal thrombotic vasculopathy. The Journal of infectious diseases. 2011;203[11]:1526-33.
84. Folgosa E, Gonzalez C, Osman NB, Hagerstrand I, Bergstrom S, Ljungh A. A case control study of chorioamniotic infection and histological chorioamnionitis in stillbirth. APMIS : acta pathologica, microbiologica, et immunologica Scandinavica. 1997;105[4]:329-36.
85. Moyo SR, Hagerstrand I, Nystrom L, Tswana SA, Blomberg J, Bergstrom S, et al. Stillbirths and intrauterine infection, histologic chorioamnionitis and microbiological findings. Int J Gynaecol Obstet. 1996;54[2]:115-23.
86. Tantbirojn P, Saleemuddin A, Sirois K, Crum CP, Boyd TK, Tworoger S, et al. Gross abnormalities of the umbilical cord: related placental histology and clinical significance. Placenta. 2009;30[12]:1083-8.
87. Altemani AM. Thrombosis of fetal placental vessels. A quantitative study in placentas of stillbirths. Pathology, research and practice. 1987;182[5]:685-9.
88. Kraus FT, Acheen VI. Fetal thrombotic vasculopathy in the placenta: cerebral thrombi and infarcts, coagulopathies, and cerebral palsy. Human pathology. 1999;30[7]:759-69.
89. Lahra MM, Gordon A, Jeffery HE. Chorioamnionitis and fetal response in stillbirth. American journal of obstetrics and gynecology. 2007;196[3]:229.e1-4.
90. Feeley L, Mooney EE. Villitis of unknown aetiology: correlation of recurrence with clinical outcome. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2010;30[5]:476-9.
91. Menghrajani P, Osterheld MC. Significance of hemorrhagic endovasculitis in placentae from stillbirths. Pathology, research and practice. 2008;204[6]:389-94.
92. Sander CM, Gilliland D, Flynn MA, Swart-Hills LA. Risk factors for recurrence of hemorrhagic endovasculitis of the placenta. Obstet Gynecol. 1997;89[4]:569-76.
93. Sander CM, Gilliland D, Richardson A, Foley KM, Fredericks J. Stillbirths with placental hemorrhagic endovasculitis: a morphologic assessment with clinical implications. Archives of pathology & laboratory medicine. 2005;129[5]:632-8.
94. Stevens NG, Sander CH. Placental hemorrhagic endovasculitis: risk factors and impact on pregnancy outcome. Int J Gynaecol Obstet. 1984;22[5]:393-7.
95. Lindam A, Johansson S, Stephansson O, Wikstrom AK, Cnattingius S. High Maternal Body Mass Index in Early Pregnancy and Risks of Stillbirth and Infant Mortality-A Population-Based Sibling Study in Sweden. American journal of epidemiology. 2016;184[2]:98-105.
96. Association between stillbirth and risk factors known at pregnancy confirmation. Jama. 2011;306[22]:2469-79.
97. Pineles BL, Hsu S, Park E, Samet JM. Systematic Review and Meta-Analyses of Perinatal Death and Maternal Exposure to Tobacco Smoke During Pregnancy. American journal of epidemiology. 2016;184[2]:87-97.
98. Crane JM, Keough M, Murphy P, Burrage L, Hutchens D. Effects of environmental tobacco smoke on perinatal outcomes: a retrospective cohort study. Bjog. 2011;118[7]:865-71.
99. Ganer Herman H, Barber E, Gasnier R, Gindes L, Bar J, Schreiber L, et al. Placental pathology and neonatal outcome in small for gestational age pregnancies with and without abnormal umbilical artery Doppler flow. European journal of obstetrics, gynecology, and reproductive biology. 2018;222:52-6.
100. Wang N, Tikellis G, Sun C, Pezic A, Wang L, Wells JC, et al. The effect of maternal prenatal smoking and alcohol consumption on the placenta-to-birth weight ratio. Placenta. 2014;35[7]:437-41.
101. Bryant AS, Worjoloh A, Caughey AB, Washington AE. Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants. American journal of obstetrics and gynecology. 2010;202[4]:335-43.
102. Agrawal A, Scherrer JF, Grant JD, Sartor CE, Pergadia ML, Duncan AE, et al. The effects of maternal smoking during pregnancy on offspring outcomes. Preventive medicine. 2010;50[1-2]:13-8.
103. Jauniaux E, Burton GJ. Morphological and biological effects of maternal exposure to tobacco smoke on the feto-placental unit. Early human development. 2007;83[11]:699-706.
104. Rowland Hogue CJ, Silver RM. Racial and ethnic disparities in United States: stillbirth rates: trends, risk factors, and research needs. Seminars in perinatology. 2011;35[4]:221-33.

105. Prather C, Fuller TR, Jeffries WLt, Marshall KJ, Howell AV, Belyue-Umole A, et al. Racism, African American Women, and Their Sexual and Reproductive Health: A Review of Historical and Contemporary Evidence and Implications for Health Equity. Health equity. 2018;2[1]:249-59.
106. Prather C, Fuller TR, Marshall KJ, Jeffries WLt. The Impact of Racism on the Sexual and Reproductive Health of African American Women. Journal of women's health [2002]. 2016;25[7]:664-71.
107. Flenady V, Koopmans L, Middleton P, Froen JF, Smith GC, Gibbons K, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet [London, England]. 2011;377[9774]:1331-40.
108. Williams AD, Wallace M, Nobles C, Mendola P. Racial residential segregation and racial disparities in stillbirth in the United States. Health & place. 2018;51:208-16.
109. Willinger M, Ko CW, Reddy UM. Racial disparities in stillbirth risk across gestation in the United States. American journal of obstetrics and gynecology. 2009;201[5]:469.e1-8.
110. Simpson LL. Maternal medical disease: risk of antepartum fetal death. Seminars in perinatology. 2002;26[1]:42-50.
111. Kishore J, Misra R, Paisal A, Pradeep Y. Adverse reproductive outcome induced by Parvovirus B19 and TORCH infections in women with high-risk pregnancy. Journal of infection in developing countries. 2011;5[12]:868-73.
112. Norbeck O, Papadogiannakis N, Petersson K, Hirbod T, Broliden K, Tolfvenstam T. Revised clinical presentation of parvovirus B19-associated intrauterine fetal death. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2002;35[9]:1032-8.
113. Tolfvenstam T, Papadogiannakis N, Norbeck O, Petersson K, Broliden K. Frequency of human parvovirus B19 infection in intrauterine fetal death. Lancet [London, England]. 2001;357[9267]:1494-7.
114. Stegmann BJ, Carey JC. TORCH Infections. Toxoplasmosis, Other [syphilis, varicella-zoster, parvovirus B19], Rubella, Cytomegalovirus [CMV], and Herpes infections. Current women's health reports. 2002;2[4]:253-8.
115. Reddy UM, Baschat AA, Zlatnik MG, Towbin JA, Harman CR, Weiner CP. Detection of viral deoxyribonucleic acid in amniotic fluid: association with fetal malformation and pregnancy abnormalities. Fetal diagnosis and therapy. 2005;20[3]:203-7.
116. Syridou G, Spanakis N, Konstantinidou A, Piperaki ET, Kafetzis D, Patsouris E, et al. Detection of cytomegalovirus, parvovirus B19 and herpes simplex viruses in cases of intrauterine fetal death: association with pathological findings. Journal of medical virology. 2008;80[10]:1776-82.
117. Van den Veyver IB, Ni J, Bowles N, Carpenter RJ, Jr., Weiner CP, Yankowitz J, et al. Detection of intrauterine viral infection using the polymerase chain reaction. Molecular genetics and metabolism. 1998;63[2]:85-95.
118. Opsjon BE, Nordbo SA, Vogt C. Unrecognized viral infections and chromosome abnormalities as a cause of fetal death - examination with fluorescence in situ hybridization, immunohistochemistry and polymerase chain reaction. APMIS : acta pathologica, microbiologica, et immunologica Scandinavica. 2017;125[9]:826-32.
119. Alvarez-Lafuente R, Aguilera B, Suarez-Mier MA, Morentin B, Vallejo G, Gomez J, et al. Detection of human herpesvirus-6, Epstein-Barr virus and cytomegalovirus in formalin-fixed tissues from sudden infant death: a study with quantitative real-time PCR. Forensic science international. 2008;178[2-3]:106-11.
120. Enders M, Weidner A, Zoellner I, Searle K, Enders G. Fetal morbidity and mortality after acute human parvovirus B19 infection in pregnancy: prospective evaluation of 1018 cases. Prenatal diagnosis. 2004;24[7]:513-8.
121. Ornoy A, Tenenbaum A. Pregnancy outcome following infections by coxsackie, echo, measles, mumps, hepatitis, polio and encephalitis viruses. Reproductive toxicology [Elmsford, NY]. 2006;21[4]:446-57.
122. Rawlinson WD, Hall B, Jones CA, Jeffery HE, Arbuckle SM, Graf N, et al. Viruses and other infections in stillbirth: what is the evidence and what should we be doing? Pathology. 2008;40[2]:149-60.
123. Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal weight, pregnancy weight gain, and the risk of antepartum stillbirth. American journal of obstetrics and gynecology. 2001;184[3]:463-9.
124. Stephansson O, Dickman PW, Johansson AL, Cnattingius S. The influence of socioeconomic status on stillbirth risk in Sweden. International journal of epidemiology. 2001;30[6]:1296-301.
125. Khong TY, Mooney EE, Ariel I, Balmus NC, Boyd TK, Brundler MA, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Archives of pathology & laboratory medicine. 2016;140[7]:698-713.
126. Redline RW, Heller D, Keating S, Kingdom J. Placental diagnostic criteria and clinical correlation--a workshop report. Placenta. 2005;26 Suppl A:S114-7.
127. Garrod A, Batra G, Ptacek I, Heazell AE. Duration and method of tissue storage alters placental morphology - implications for clinical and research practice. Placenta. 2013;34[11]:1116-9.
128. Genest DR. Estimating the time of death in stillborn fetuses: II. Histologic evaluation of the placenta; a study of 71 stillborns. Obstet Gynecol. 1992;80[4]:585-92.
129. Sun CC, Revell VO, Belli AJ, Viscardi RM. Discrepancy in pathologic diagnosis of placental lesions. Archives of pathology & laboratory medicine. 2002;126[6]:706-9.
130. Christians JK GD. Placental villous hypermaturation is associated with improved neonatal outcomes. Placenta. 2019;76:1-5.
131. Huynh J, Dawson D, Roberts D, Bentley-Lewis R. A systematic review of placental pathology in maternal diabetes mellitus. Placenta. 2015;36[2]:101-14.
132. Evers IM, Nikkels PG, Sikkema JM, Visser GH. Placental pathology in women with type 1 diabetes and in a control group with normal and large-for-gestational-age infants. Placenta. 2003;24[8-9]:819-25.
133. Daskalakis G, Marinopoulos S, Krielesi V, Papapanagiotou A, Papantoniou N, Mesogitis S, et al. Placental pathology in women with gestational diabetes. Acta obstetricia et gynecologica Scandinavica. 2008;87[4]:403-7.
134. Al-Adnani M, Marnerides A, George S, Nasir A, Weber MA. "Delayed Villous Maturation" in Placental Reporting: Concordance among Consultant Pediatric Pathologists at a Single Specialist Center. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2015;18[5]:375-9.
135. Seidmann L, Suhan T, Kamyshanskiy Y, Nevmerzhitskaya A, Gerein V, Kirkpatrick CJ. CD15 - a new marker of pathological villous immaturity of the term placenta. Placenta. 2014;35[11]:925-31.
136. Seidmann L, Anspach L, Roth W. The embryo-placental CD15-positive "vasculogenic zones" as a source of propranolol-sensitive pediatric vascular tumors. Placenta. 2016;38:93-9.
137. Seidmann L, Suhan T, Unger R, Gerein V, Kirkpatrick CJ. Transient CD15-positive endothelial phenotype in the human placenta correlates with physiological and pathological fetoplacental immaturity. European journal of obstetrics, gynecology, and reproductive biology. 2014;180:172-9.

138. Mukherjee A, Chan AD, Keating S, Redline RW, Fritsch MK, Machin GA, et al. The Placental Distal Villous Hypoplasia Pattern: Interobserver Agreement and Automated Fractal Dimension as an Objective Metric. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2016;19[1]:31-6.
139. Redline RW. Maternal Vascular Malperfusion. In: Raymond w Redline TKB, Drucilla J Roberts, editor. Placental and Gestational Pathology. Diagnostic Pediatric Pathology. Cambridge: Cambridge University Press; 2018.
140. Benirschke K, Kaufmann P, Baergen R. Pathology of the Human Placenta. 5th ed: Springer Science and Business Media,Inc.; 2006.
141. Singer DB. The placenta in pregnancies complicated by diabetes mellitus. Perspectives in pediatric pathology. 1984;8[3]:199-212.



Faulty Placentation of Maternal Vessels and Placental Dysfunction: a Window to the Future Health of Mothers

Dr M. Kashif Mohiuddin
MD [Pathology], DipRCPath
Consultant Pathologist, Krishna Institute of Medical Sciences, Secunderabad, Telangana, India. Member,Perinatal Pathology Committee, Stillbirth Society of India

Dr Sunil Jaiman
Section Head, Placental Pathology Perinatology Research Branch, NICHD. Assistant Professor, Dept. Of Pathology, Hutzel Women's Hospital, Wayne State University School of Medicine, Detroit, MI, USA, Chairman Perinatal Pathology Committee, Stillbirth Society of India

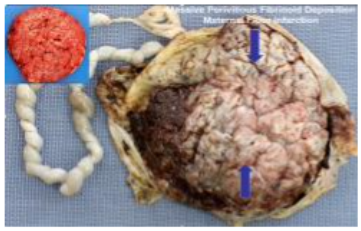
Aims and Objectives:
To determine the frequency and type of histopathologic lesions in placentas delivered by women at our center and to ascertain how faulty placentation of maternal vessels and placental dysfunction affects the future health of mothers.

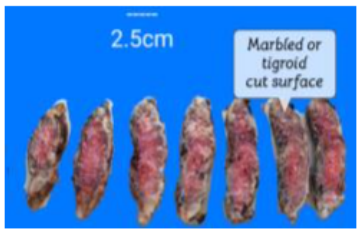
Materials and Methods:
A retrospective study of twenty-one consecutive placentas from women who delivered at KIMS was conducted. Amsterdam Placental Workshop Group Consensus Statement was deployed for the morphological analysis of the placentas (1) . Formalin-fixed paraffin-embedded (FFPE) placental tissue sections were stained with Hematoxylin & Eosin..

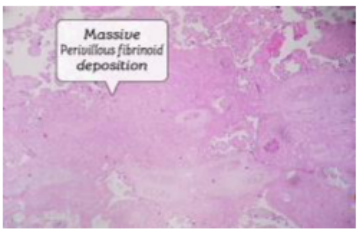
Results:
Placental pathology showed the following lesions in the decreasing order of frequency: maternal and fetal vascular malperfusion [42.85% (9/21)], placenta accreta spectrum [19.04% (4/21)], acute inflammatory lesions of the placenta [14.28% (3/21)], massive perivillous fibrinoid deposition [9.52% (2/21)], chronic histiocytic Intervillositis [4.76% (1/21)], delayed villous maturation [4.76% (1/21)], and complete hydatidiform mole [4.76% (1/21)].

This poster was presented in the Annual Conference of Hyderabad, Academy of Pathologists, September 23-26, 2021, 2-5pm IST. The poster was awarded first prize. It is being published here for wider dissemination of knowledge. (https://hydacpath.wordpress.com/2021/08/16/hap-online-meeting-2021/)

Massive Perivillous Fibrinoid Deposition

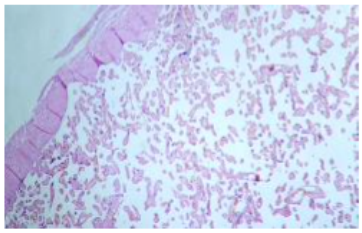




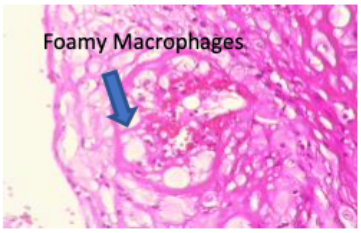


Maternal Vascular Malperfusion

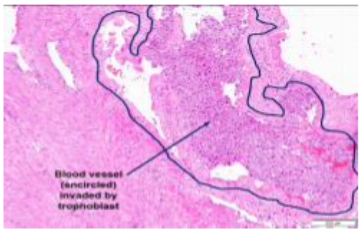
Distal villous Hypoplasia



Acute atherosis

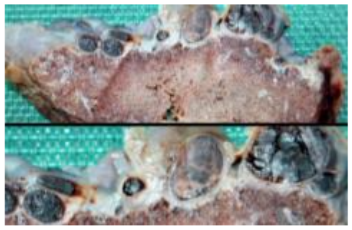


Endovascular trophoblasts



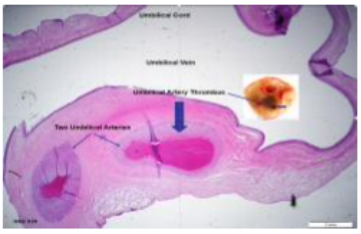
Fetal Vascular Malperfusion

Occlusive mural thrombi

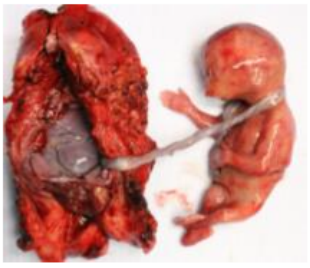


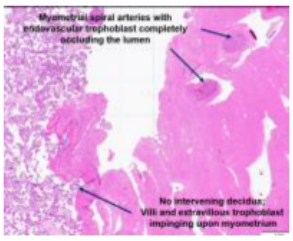
Intimal fibrin cushion

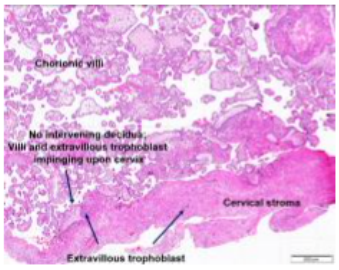
Occlusive mural thrombi



Placenta Accreta Spectrum

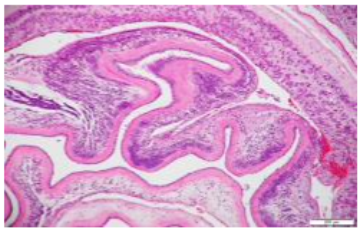




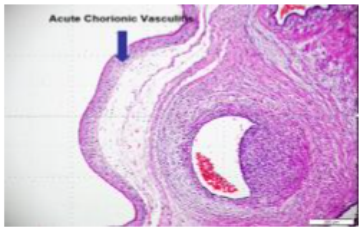


Placenta Inflammatory Lesions

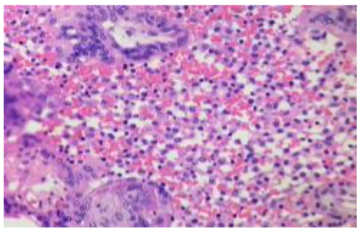
Acute chorioamnionitis



Acute chorionic vasculitis



Chronic histiocytic intervillositis



Dr. Kashif M, Dr. Jaiman S (https://hydacpath.wordpress.com/2021/08/16/hap-online-meeting-2021/)

Faulty Placentation of Maternal Vessels and Placental Dysfunction

A Window to Future Health of Mothers & Babies

Dr Sunil Jaiman
MD, DipRCPath [UK], FCAP [USA]
Section Head, Placental Pathology Perinatology Research Branch, NICHD.
Assistant Professor, Dept. Of Pathology, Hutzel Women's Hospital, Wayne State University School of Medicine, Detroit, MI, USA, Chairman Perinatal Pathology Committee, Stillbirth Society of India

Placenta Nomenclature and Historical Aspects

In the Old Testament, the organ was referred to as the "Seat of the External Soul" or the "Bundle of Life." Other cultural interpretations of the placenta have included its role as a companion to the child or another soul that can serve to warn the child of danger or act as a conscience. [Loke YW. Life's vital link: the astonishing role of the placenta, 1st ed. Oxford, UK: Oxford University Press; 2013; Long EC. The Placenta in Lore and Legend. Bulletin of the Medical Library Association. 1963;51[2]:233-241]

Development of the placenta is precocious because the organ must be ready and able to support the fetus [1]. Superficially the human placenta is recognizable as the discoid structure that interfaces with the mother, but is in fact remarkably difficult to define biologically [1-3]

- No organ can match the placenta for the diversity of its functions because it performs the actions of all the major organ systems while these are differentiating and maturing in the fetus
- There is an astonishing range of morphological variations in placental types seen across mammals and even lower orders

[Wooding FP, Burton GJ. Comparative Placentation. structures, functions and evolution. Berlin [Germany]: Springer; 2008]

Current Definition of Placenta

Mossman first attempted to simplify the matters by stating that "the normal mammalian placenta is an apposition or fusion of the fetal membranes to the uterine mucosa for physiological exchange" [4]. Burton and Jauniaux [1] define the placenta as an extracorporeal organ that interacts with the endometrium to nourish and protect the fetus and orchestrates maternal adaptations to pregnancy [1]. Despite the semantics of placental definition, what is clear is that placenta has two components: a fetal and a maternal one that must interact successfully for a healthy pregnancy.

The Concept of Fetal and Maternal Components and the Immunological Problem of Pregnancy

This concept of fetal and maternal components and the immunological problem of pregnancy was first promulgated by Sir Medawar [5, 6] who questioned: how does the pregnant mother contrive to nourish within itself, for many weeks or months, a fetus that is an antigenically foreign body?''

Late Sir Peter Brian Medawar made a pivotal contribution in 1953 by establishing the field of Reproductive Immunology and elucidated the mechanisms responsible for the paradoxical survival of the conceptus as an intra-uterine allograft within the immunologically competent genetically alien female host. Medawar's succinct and stimulating theories have been central throughout the past fifty years and his basic conclusion, that the single most important factor ensuring the success of gestation is the anatomical separation of the fetus from its mother, remains substantially valid to this day [7].

"The mysterious lack of rejection of the fetus has puzzled generations of immunologists, and no comprehensive explanation has yet emerged. One problem is that acceptance of the fetal allograft is so much the norm that it is difficult to study the mechanism that prevents rejection: if the mechanism for rejecting the fetus is rarely activated, how can one analyze the mechanism that controls it?"

Placental Dysfunction: a Window to the Future Health of the Mothers and the Babies

How Is Placental Dysfunction a Window to the Future Health of Mothers?

Cardiovascular Health and Maternal Placental Syndromes [CHAMPS], population-based retrospective cohort study reported that the risk of premature cardiovascular disease is higher after a maternal placental syndrome, especially in the presence of fetal compromise. Affected women should have their blood pressure and weight assessed about 6 months postpartum, and a healthy lifestyle should be emphasized [19].

Pregnancies complicated by placental abruption or infarction, pre-eclampsia, intrauterine growth restriction, gestational hypertension or intrauterine fetal death correlated positively with an increased risk for the diagnosis of cardiovascular disease more than a decade after the index pregnancy [17, 18]. Importantly, the absolute risk was still low, but the relative risk was substantially higher than for women without previous pregnancy complications [17, 18].

How Does the Placenta Contribute to Maternal Long- Term Risk?

Women who experience some placental dysfunction disorders may be predisposed to long-term adverse outcomes before pregnancy, with pregnancy offering a stress test to their organs that brings out an inherent risk [17]. Alternatively, placental disorders may have long-lasting, if not permanent, effects on the mother's physiologic condition, moving the threshold for disease to a lower level than the threshold exhibited by women with uncomplicated pregnancies [17].

Perhaps a mixture of these concepts is tenable. The truth remains to be proven. It is known that placental "communications" with the mother are multiple and persistent. Cell-free fetal DNA in the maternal circulation is likely from trophoblast; exosomes, microparticles, and fragments from trophoblast are detected in the maternal blood stream. Many hormones, cytokines, and growth factors that are secreted by the placenta differentially appear in high concentrations in the maternal circulation [e.g., human chorionic gonadotropin and human placental lactogen]

"The mysterious lack of rejection of the fetus has puzzled generations of immunologists, and no comprehensive explanation has yet emerged. One problem is that acceptance of the fetal allograft is so much the norm that it is difficult to study the mechanism that prevents rejection: if the mechanism for rejecting the fetus is rarely activated, how can one analyse the mechanism that controls it?"

Ken Murphy [Eds.], Janeway's Immunobiology Textbook - 8th Edition Garland Science, New York, 2008

How Is Placental Dysfunction a Window to the Future Health of Babies?

Barker was the first to promote aggressively the concept that in utero programming increased the risk for adverse health outcomes in offspring later in life [11].Barker hypothesis was that some placental phenotypes were predictive of an increased long-term risk for hypertension and cardiovascular diseases, among other conditions [11] However, the Developmental Origins of Health and Disease, offers the premise that in utero programming influences health or maladies later in life, independent of the DNA sequences that are inherited in a person's genetic code [17].

In-utero alterations in hypothalamic-pituitary function, kidney development or substrate metabolism, to name a few, can each have long- lasting effects on health risks for the offspring reaching adulthood [11, 17, 20, 21]. Whether directly or indirectly, placental dysfunction is pivotal in creation of the environment to which the fetus responds with programming changes [11, 17, 20, 21]

Clinical and Research Implications of Placental Dysfunction in Fetal Death

The use of objective data, i.e., clinical information, placental examination, and fetal autopsy, to assess the causes of fetal death allows for the identification of potential etiologies of fetal death in 40% of the cases [22]. Given that the risk factors for stillbirth are also present in live-born neonates, one cannot attribute the presence of these risk factors as direct causes of fetal death [23]. In one study it was shown that 56% of the cases with fetal death had more than one risk factor, and 92% of placentas from antenatal fetal death showed pathologic findings [24]. The Stillbirth Collaborative Research Network reported that 31% of fetal deaths that occurred among 59 tertiary care and community hospitals from 2006 to 2008 had more than one probable or possible cause of death [25].

These two studies support the notion that the cause of death is multifactorial. Because multiple conditions may contribute to a stillbirth, the practice of recording the chain of events that lead to death, rather than the single-most probable cause of death, is recommended [23, 26, 27].

Studies that included a large population of singleton pregnancies demonstrated that the lowest rate of stillbirth in pregnancy occurs in fetuses whose birthweight centile is above the mean or the 50th percentile [28-32]. Furthermore, it has been shown that pregnancies that resulted in antepartum fetal death had significantly lower growth velocities of fetal head circumference, biparietal diameter, abdominal circumference, femur length and estimated fetal weight [EFW] compared to pregnancies that delivered a liveborn neonate [32]. The clinical implications being that assessment of fetal growth velocity doubles the detection rate of antepartum fetal death compared to a single estimated fetal weight [EFW] measurement at the last available ultrasound scan before diagnosis of demise. Fetuses with EFW growth velocity < 10th percentile value of pregnancies with a live birth had a 9.4-fold and 11.2-fold increased risk of antepartum death [32].

Although there is no clinical or placental histopathologic consensus on the definition of placental dysfunction, data suggests that characteristics of placental dysfunction may include an estimated fetal weight <50th percentile determined by ultrasound in association with specific gross placental characteristics and placental histologic lesions [24, 33].

Velamentous cord insertion [34-39], hypercoiling of the cord [34, 36, 40-44], true tight knots [35, 36, 40, 41, 43, 45], and shape abnormalities [46] have been reported to contribute to fetal death. Velamentous cord insertion has been reported as a risk factor for stillbirth in early preterm delivery, associated with congenital anomalies and twin gestation [47].

The birthweight and placental weight may get affected by a prolonged death-to-delivery time interval [48, 49]. The feto-placental weight ratio however remain the same because the fetus and placenta not only share the same intrauterine environment [50] but constitute a single morphological and functional unit [51]. Indeed, the feto-placental weight ratio of fetal death has been shown to be significantly lower than that for controls [24]. Notably, in 68% of the cases, the estimated fetal weight determined by ultrasound was <50th percentile for gestational age at the last examination when the fetus was alive [24].

Conclusion

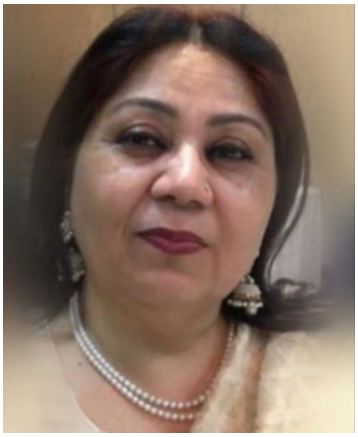
Utilizing the aforementioned definition, placental dysfunction seems to be the underlying cause of death in 84% of the cases [24]. Further research and prospective studies are warranted to validate this concept of placental dysfunction. Current placental pathological examination relies on limited sampling of a large organ. Moreover, placental morphologic criteria are largely subjective and qualitative. Perhaps time is ripe for applying molecular and digital pathology techniques to address the complex lesions of placenta, especially in the context of stillbirth.

References

1.Burton GJ, Jauniaux E. What is the placenta? American journal of obstetrics and gynecology. 2015;213[4 Suppl]:S6.e1, S6-8.
2.Burton GJ, Fowden AL. The placenta: a multifaceted, transient organ. Philosophical transactions of the Royal Society of London Series B, Biological sciences. 2015;370[1663]:20140066.
3.Burton GJ, Fowden AL, Thornburg KL. Placental Origins of Chronic Disease. Physiological reviews. 2016;96[4]:1509-65.
4.Mossman HW. Classics revisited: Comparative morphogenesis of the fetal membranes and accessory uterine structures. Placenta. 1991;12[1]:1-5.
5.Medawar PB. The immunology of transplantation. Harvey lectures. 1956[Series 52]:144-76.
6.Medawar PB. Immunological tolerance. Nature. 1961;189:14-7.
7.Billington WD. The immunological problem of pregnancy: 50 years with the hope of progress. A tribute to Peter Medawar. Journal of reproductive immunology. 2003;60[1]:1-11.
8.Barker DJ. Maternal nutrition, fetal nutrition, and disease in later life. Nutrition [Burbank, Los Angeles County, Calif]. 1997;13[9]:807-13.
9.Barker DJ. The developmental origins of adult disease. Journal of the American College of Nutrition. 2004;23[6 Suppl]:588s-95s.
10.Barker DJ. The origins of the developmental origins theory. Journal of internal medicine. 2007;261[5]:412-7.
11.Barker DJ, Bull AR, Osmond C, Simmonds SJ. Fetal and placental size and risk of hypertension in adult life. BMJ [Clinical research ed]. 1990;301[6746]:259-62.
12.Barker DJ, Larsen G, Osmond C, Thornburg KL, Kajantie E, Eriksson JG. The placental origins of sudden cardiac death. International journal of epidemiology. 2012;41[5]:1394-9.
13.Barker DJ, Osmond C, Thornburg KL, Kajantie E, Eriksson JG. The lifespan of men and the shape of their placental surface at birth. Placenta. 2011;32[10]:783-7.
14.Barker DJ, Thornburg KL. Placental programming of chronic diseases, cancer and lifespan: a review. Placenta. 2013;34[10]:841-5.
15.Barker DJ, Thornburg KL, Osmond C, Kajantie E, Eriksson JG. Beyond birthweight: the maternal and placental origins of chronic disease. Journal of developmental origins of health and disease. 2010;1[6]:360-4.
16.Fraser A, Nelson SM, Macdonald-Wallis C, Cherry L, Butler E, Sattar N, et al. Associations of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: the Avon Longitudinal Study of Parents and Children. Circulation. 2012;125[11]:1367-80.
17.Nelson DM. How the placenta affects your life, from womb to tomb. American journal of obstetrics and gynecology. 2015;213[4 Suppl]:S12-3.
18.Sattar N, Greer IA. Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening? BMJ [Clinical research ed]. 2002;325[7356]:157-60.
19.Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes [CHAMPS]: population-based retrospective cohort study. Lancet [London, England]. 2005;366[9499]:1797-803.
20.Lucas A. Role of nutritional programming in determining adult morbidity. Archives of disease in childhood. 1994;71[4]:288-90.
21.McMillen IC, Robinson JS. Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. Physiological reviews. 2005;85[2]:571-633.
22.Man J, Hutchinson JC, Heazell AE, Ashworth M, Jeffrey I, Sebire NJ. Stillbirth and intrauterine fetal death: role of routine histopathological placental findings to determine cause of death. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2016;48[5]:579-84.
23.Silver RM, Varner MW, Reddy U, Goldenberg R, Pinar H, Conway D, et al. Work-up of stillbirth: a review of the evidence. American journal of obstetrics and gynecology. 2007;196[5]:433-44.
24.Jaiman S, Romero R, Pacora P, Jung E, Bhatti G, Yeo L, et al. Disorders of placental villous maturation in fetal death. Journal of perinatal medicine. 2020.
25.Bukowski R CM, Conway D, Coustan D, Dudley DJ, Goldenberg RL, Hogue CJ, Koch MA, Parker CB, Pinar H, Reddy UM, Saade GR, Silver RM, Stoll BJ, Varner MW, Willinger M. Causes of death among stillbirths. Jama. 2011;306[22]:2459-68.
26.Froen JF, Pinar H, Flenady V, Bahrin S, Charles A, Chauke L, et al. Causes of death and associated conditions [Codac]: a utilitarian approach to the classification of perinatal deaths. BMC pregnancy and childbirth. 2009;9:22.
27.Flenady V, Froen JF, Pinar H, Torabi R, Saastad E, Guyon G, et al. An evaluation of classification systems for stillbirth. BMC pregnancy and childbirth. 2009;9:24.
28.Vangen S, Stoltenberg C, Skjaerven R, Magnus P, Harris JR, Stray-Pedersen B. The heavier the better? Birthweight and perinatal mortality in different ethnic groups. International journal of epidemiology. 2002;31[3]:654-60.
29.Francis JH, Permezel M, Davey MA. Perinatal mortality by birthweight centile. The Australian & New Zealand journal of obstetrics & gynaecology. 2014;54[4]:354-9.
30.Ray JG, Urquia ML. Risk of stillbirth at extremes of birth weight between 20 to 41 weeks gestation. Journal of perinatology : official journal of the California Perinatal Association. 2012;32[11]:829-36.
antepartum fetal death. Ultrasound in Obstetrics & Gynecology. 2021.

31.Vasak B, Koenen SV, Koster MP, Hukkelhoven CW, Franx A, Hanson MA, et al. Human fetal growth is constrained below optimal for perinatal survival. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2015;45[2]:162-7.
32.Pacora P, Romero R, Jung E, Gudicha D, Hernandez-Andrade E, Musilova I, et al. Reduced fetal growth velocity precedes antepartum fetal death. Ultrasound in Obstetrics & Gynecology. 2021.
33.Pacora P, Romero R, Jung E, Gudicha DW, Hernandez-Andrade E, Musilova I, et al. Reduced fetal growth velocity precedes antepartum fetal death. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2020.
34.Hovatta O, Lipasti A, Rapola J, Karjalainen O. Causes of stillbirth: a clinicopathological study of 243 patients. British journal of obstetrics and gynaecology. 1983;90[8]:691-6.
35.Amir H, Weintraub A, Aricha-Tamir B, Apel-Sarid L, Holcberg G, Sheiner E. A piece in the puzzle of intrauterine fetal death: pathological findings in placentas from term and preterm intrauterine fetal death pregnancies. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2009;22[9]:759-64.
36.VanderWielen B, Zaleski C, Cold C, McPherson E. Wisconsin stillbirth services program: a multifocal approach to stillbirth analysis. American journal of medical genetics Part A. 2011;155a[5]:1073-80.
37.Pinar H, Goldenberg RL, Koch MA, Heim-Hall J, Hawkins HK, Shehata B, et al. Placental findings in singleton stillbirths. Obstet Gynecol. 2014;123[2 Pt 1]:325-36.
38.Gibbins KJ, Silver RM, Pinar H, Reddy UM, Parker CB, Thorsten V, et al. Stillbirth, hypertensive disorders of pregnancy, and placental pathology. Placenta. 2016;43:61-8.
39.Bukowski R, Hansen NI, Pinar H, Willinger M, Reddy UM, Parker CB, et al. Altered fetal growth, placental abnormalities, and stillbirth. PLoS One. 2017;12[8]:e0182874.
40.Korteweg FJ, Erwich JJ, Holm JP, Ravise JM, van der Meer J, Veeger NJ, et al. Diverse placental pathologies as the main causes of fetal death. Obstet Gynecol. 2009;114[4]:809-17.
41.Horn LC, Langner A, Stiehl P, Wittekind C, Faber R. Identification of the causes of intrauterine death during 310 consecutive autopsies. European journal of obstetrics, gynecology, and reproductive biology. 2004;113[2]:134-8.
42.Ogunyemi D, Jackson U, Buyske S, Risk A. Clinical and pathologic correlates of stillbirths in a single institution. Acta obstetricia et gynecologica Scandinavica. 1998;77[7]:722-8.
43.Bar J, Schreiber L, Ben-Haroush A, Ahmed H, Golan A, Kovo M. The placental vascular component in early and late intrauterine fetal death. Thrombosis research. 2012;130[6]:901-5.
44.Chang KT, Keating S, Costa S, Machin G, Kingdom J, Shannon P. Third-trimester stillbirths: correlative neuropathology and placental pathology. Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society. 2011;14[5]:345-52.
45.Bonetti LR, Ferrari P, Trani N, Maccio L, Laura S, Giuliana S, et al. The role of fetal autopsy and placental examination in the causes of fetal death: a retrospective study of 132 cases of stillbirths. Arch Gynecol Obstet. 2011;283[2]:231-41.
46.Longtine MS, Nelson DM. Placental dysfunction and fetal programming: the importance of placental size, shape, histopathology, and molecular composition. Seminars in reproductive medicine. 2011;29[3]:187-96.
47.Yerlikaya G, Pils S, Springer S, Chalubinski K, Ott J. Velamentous cord insertion as a risk factor for obstetric outcome: a retrospective case-control study. Arch Gynecol Obstet. 2016;293[5]:975-81.
48.Man J, Hutchinson JC, Ashworth M, Heazell AE, Levine S, Sebire NJ. Effects of intrauterine retention and postmortem interval on body weight following intrauterine death: implications for assessment of fetal growth restriction at autopsy. Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2016;48[5]:574-8.
49.Strachan GI. THE PATHOLOGY OF FOETAL MACERATION : A STUDY OF 24 CASES. British medical journal. 1922;2[3211]:80-2.
50.Haavaldsen C, Samuelsen SO, Eskild A. Fetal death and placental weight/birthweight ratio: a population study. Acta obstetricia et gynecologica Scandinavica. 2013;92[5]:583-90.
51.Mecacci F, Serena C, Avagliano L, Cozzolino M, Baroni E, Rambaldi MP, et al. Stillbirths at Term: Case Control Study of Risk Factors, Growth Status and Placental Histology. PLoS One. 2016;11[12]:e0166514.

Secretary's Report



Dr. Tamkin Khan

Professor ObGyn, JNMCH
Founder Secretary
Stillbirth Society of India

Last month, we witnessed the historic online inauguration of the Stillbirth Society of India, held on 13th August, 2021. The event enlightened us on the mission and vision of the society under the eminent leadership and guidance of the President, Dr. Neelam Aggarwal, Vice President Dr. Nuzhat Aziz and Secretary Dr. Tamkin Khan.

The event started with a welcome address by Dr. Asna Ashraf [Consultant ObGyn, Ujala Medical Centre, Lucknow] Founder Member and Joint Secretary of the Society. Dr. Asna was the Master of Ceremonies for the event and conducted the session.

Dr. Neelam Aggarwal [Professor, ObGyn, PGI Chandigarh], Founder President SBSI gave the Presidential Address on the problem statement, mission and vision of the society and highlighted the importance of increasing awareness on stillbirth prevention, quality care during pregnancy and childbirth, bereavement care and measuring the data on stillbirths.

Dr. Nuzhat Aziz [Consultant ObGyn, Fernandez Hospitals, Hyderabad], Founder Vice President SBSI, gave an inspiring talk on intrapartum stillbirths and how the labour room care can be optimised.

Dr. Tamkin Khan [Professor, ObGyn, JNMCH, AMU], Founder Secretary of the society introduced Stillbirth Society of India, how it came into existence, the different committees and future plans.

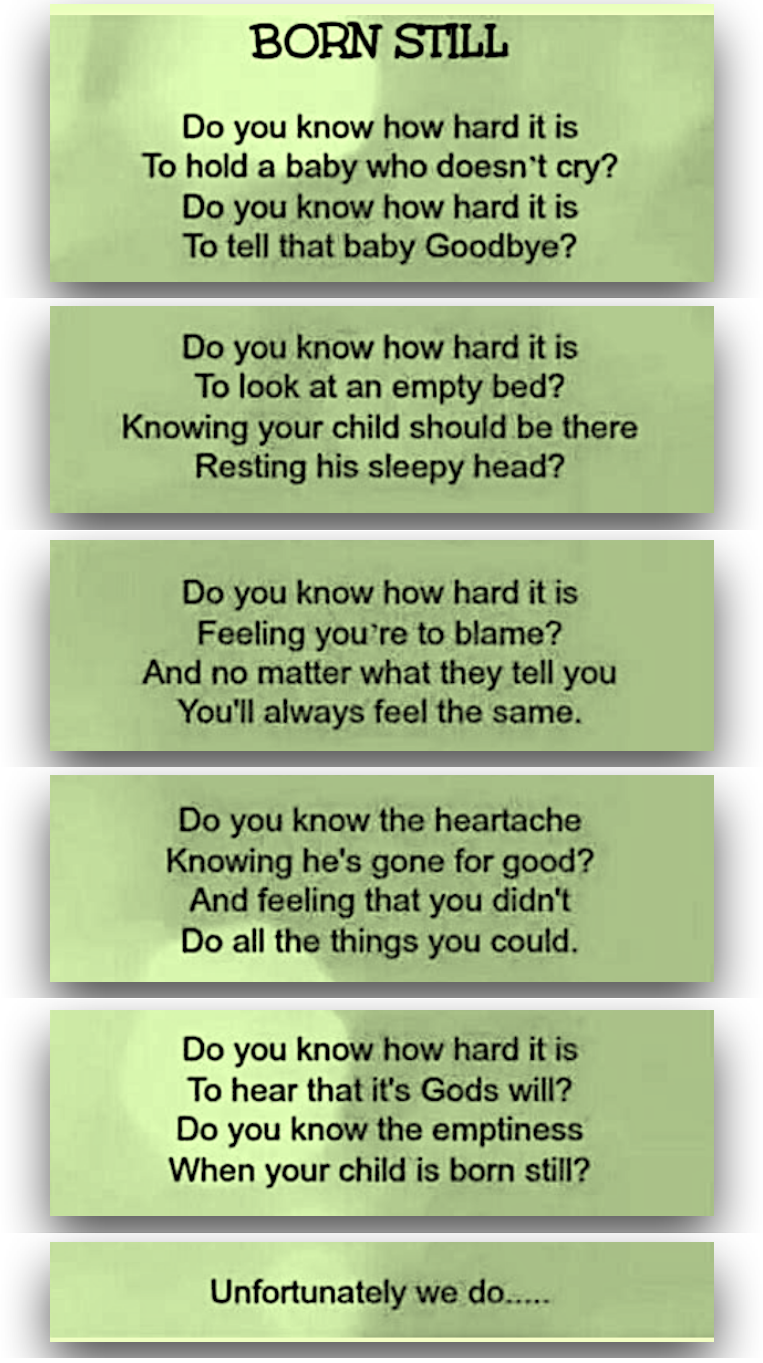
The Keynote by international expert Susannah Hopkins Leisher, Board Chair, International Stillbirth Alliance gave an insight into the magnitude of the problem on the global front and encouraged all the global bodies to come together for the cause and maintain the continuum of care.

The Guest of Honour Dr. Padmini Kashyap, Assistant Commissioner [Maternal Health] Ministry of Health and Family Welfare [MOHFW], Government of India [GOI] focussed on improving intrapartum quality of care for preventing stillbirths elaborating the measures taken by the GOI to achieve the plausible targets.

Chief Guest for the event Dr Sumita Ghosh, Additional Commissioner [Child Health, Adolescent Health, RBSK, MOHFW, GOI] brought forward the sensitivity of the issue of prevention of stillbirths and mentioned profoundly that 'every stillbirth is a baby lost'.

The session ended with a vote of thanks delivered by Dr. Ayesha Ahmad [Associate Professor, ObGyn, ELMCH, Lucknow], Founder Member and Joint Secretary of the Society.

The event was a success and an enormous boost to the untiring efforts and far sighted vision of the board members to make a difference in the existing scenario. With the mission to decrease the incidence and the impact of stillbirth, we fervently hope and pledge to live up to the motto of SBSI, **" Preventing death before birth"**



Author: Unknown

Retrieved from: https://minutebyminute1.wordpress.com/2019/10/01/day-29-one-stillbirth-quote-that-i-love/

October 2021 Calendar

Theme of the Month: Recurrent Pregnancy Loss