



A Review of Placental Pathology of Stillbirths at a Tertiary Centre in the Himalayan Region

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Abstract

The largest proportion of the world's stillbirths are contributed by India. Studies on the histopathological spectrum of findings in the placenta of stillbirths are relatively less particularly in the extensive Himalayan region of India. At a tertiary care hospital in Himachal Pradesh, we assessed the spectrum of findings in 94 placentas of stillbirths over a period of one year. We observed that 76.59% of mothers belonged to the 20 to 30 years age group and 63.80% stillborns were males. While a normal study constituted only roughly 40% on gross and histopathological examination, 26.59% revealed acute chorioamnionitis and 13.82% had acute funisitis, highlighting the prevalent role of infectious causes leading to stillbirths even today. 10.63% showed infarcted chorionic villi and 8.50% cases had thrombotic vasculopathy. Further elucidation of the causes leading to the same and correction of the preventable ones still remain extremely necessary.

Introduction

Stillbirth has not been accounted for globally as part of major maternal and child health strategies, yet it is one of the most common albeit poorly studied adverse pregnancy outcomes.⁽¹⁾⁽²⁾ According to WHO, a stillbirth is a baby born with no signs of life after a specific threshold, with early stillbirths occurring at 22 to 27 completed gestational weeks and late stillbirth at 28 weeks or more of gestation.⁽³⁾

A 2019 UN report further highlighted India's leading position in countries with the maximum

number of stillbirths, surprisingly, bearing almost half of the burden along with Pakistan, Nigeria, Congo, China and Ethiopia.⁽³⁾ The present still-birth rate of Himachal Pradesh in northern Indian himalayan region is 10 per 1000 live births.⁽⁴⁾

The placenta is often considered as the "black box" of pregnancy and a detailed examination gives insight into the preceding maternal and fetal events.⁽¹³⁾ We attempted to examine and assess the histopathological findings in all cases of stillbirths in our institution over a period of one year.

Aim

To determine the histopathological spectrum of findings observed in placenta in all cases of stillbirths.

Materials and Methods

A retrospective study was conducted in the Department of Pathology, Indira Gandhi Medical College, a tertiary care centre and government hospital in Shimla, Himachal Pradesh. A total of 94 cases of stillbirths were assessed during the period from 1st August 2015 to 31st July 2016.

All the antepartum and intrapartum stillbirths were enrolled.

Inclusion Criteria

All the subjects regardless of their booking status who delivered stillborn were included in this study. Stillbirth at >20 weeks (if gestational age was known), or weight ≥ 500 gm (if gestational age was not known) were included in the study. Both singleton and multiple pregnancies were included in the study.

Exclusion Criteria

Women diagnosed with intrauterine demise but planning to deliver outside were excluded from the study. Gestational age was estimated by: first day of last menstrual period when reliable and/or early USG imaging before 20 weeks of gestation. Demographic data, age, parity, level of literacy, socioeconomic status, booking status were noted. Detailed history was taken regarding various obstetric risk factors in current pregnancy. This was followed by general physical examination, BMI calculation and systemic examination. Apart from routine investigations of pregnancy, the following specific investigations were done in order to find out the ethology of intrauterine/intrapartum fetal death:

- Suspected hypertension related disease: Complete hemogram, renal function test with uric acid levels, liver function test, urine albumin, 24-hour urinary protein, fundus.
- Suspected diabetes-related disease, macrosomia (history), a strong family his-

tory of diabetes, or obesity: HbA1c, Blood Sugar Profile.

- Suspected fetal hydrops: antibody screening, parvovirus B19 serology, Rh status and ICT in Rh incompatibility and haemoglobin electrophoresis.
- Suspected chorioamnionitis: Total leukocyte count (TLC), Differential leukocyte count (DLC), C- reactive protein (CRP), vaginal swab c/s and placental membranes were sent for culture and histopathological examination.
- IUFD with fever: septic screen i.e TLC, CRP, slide for malarial parasite, Widal test, Weil Felix, Urine microscopic examination and culture, Endocervical swab for culture and sensitivity, Placental membrane for culture and sensitivity.
- Coagulogram and platelet count to rule out coagulopathy. Written informed consent for labor was taken.

Collection of Placenta: Universal precautions were observed. Placentas were examined soon after delivery. They were thoroughly washed to remove the blood clots and sent to the pathology laboratory immersed in 10% neutral buffered formalin in a sterile container. At the pathology department, the following features were recorded:

Weight: Placental weight including cord and membranes was taken after removing any retroplacental clot from the maternal surface.

Dimensions of the placenta: Three dimensions were noted with a non stretchable tape.

Gross examination of the placenta: The fetal and the maternal surfaces were examined for any gross abnormalities.

Umbilical Cord Examination: The cord was measured using a non-stretchable tape; any abnormalities were recorded.

Examination of the Membranes: The membranes were examined for any abnormalities. Appropriate sections were taken followed by tissue processing and hematoxylin and eosin staining.⁽⁵⁾

The slides were examined by the pathologist and the findings recorded.

Statistical Analysis: Significance of difference was analysed using unpaired student t test. Statistical analysis was done using statistical software Epi info version 7.

Observations

The following observations were noted: 94 stillbirths occurred over the study period of one year, accounting to a stillbirth rate of 14.66 per 1000 live births. Majority of patients (76.59%) belonged to the 20n to 30 years age group. While 14.89% of mothers were aged above 30 years, on-

ly 8.50% cases were aged less than 20 years. 63.80% stillborns were of male gender. On both gross and histopathological examination, a normal study was noted in 41.59% and 40.45% cases respectively. A subchorionic hematoma was observed in 31.91% cases followed by grossly evident necrosis in 25.50%. However, this was not statistically significant. On histopathological examination of the placenta, acute chorioamnionitis was observed in 26.59% and acute funisitis in 13.82%. Infarcted chorionic villi was seen in 10.63% and the least common finding was of thrombotic vasculopathy in 8.50%.

Table 1: Number of stillbirths and the stillbirth rate

Total deliveries	6412
Total number of stillbirths	94
Stillbirth rate	14.66/1000 live births

Table 2: Age of mothers in our study

Age of mother	Number of stillbirths	Percentage
<20 years	8	8.50%
20-30 years	72	76.59%
>30 years	14	14.89%

Table 3: Sex of stillborns in our study

Sex of stillborn	Number	Percentage
Male	60	63.80%
Female	34	36.20%

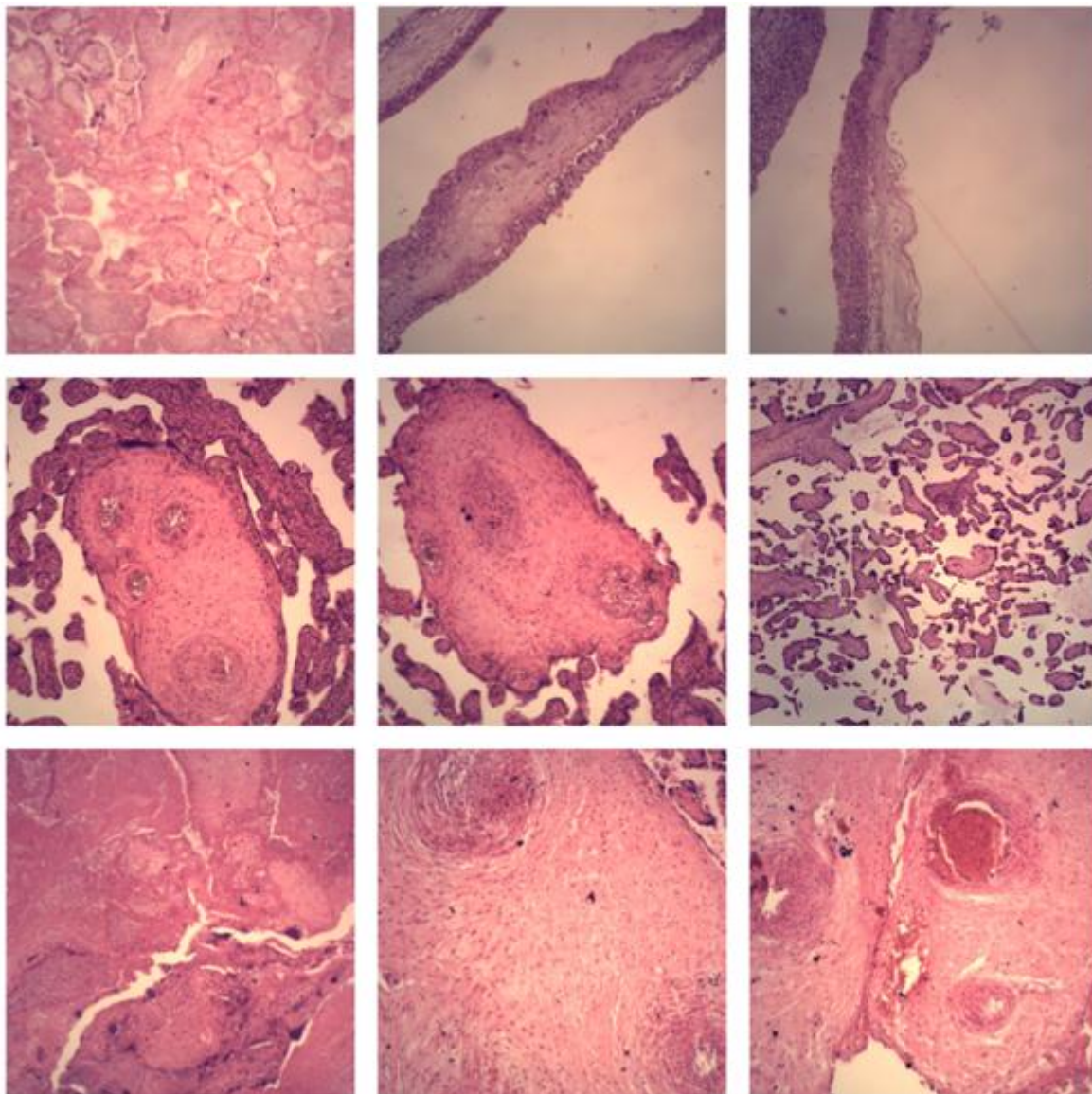
Table 4: Gross pathological findings

Gross Placental Examination	Number	Percentage
Subchorionic haematoma	30	31.91%
Necrosis	24	25.50%
Normal study	40	41.59%

Table 5: Histopathological findings

Histopathological placental examination		
Infarcted chroionic villi	10	10.63%
Thrombotic vasculopathy	8	8.50%
Acute funisitis	13	13.82%
Acute chorioamnionitis	25	26.59%
Normal study	38	40.45%

Figure.1: (Left to right) Top row: Infarcted chorionic villi, and changes of acute chorioamnionitis. Middle row: Acute funisitis and variably sized and fibrosed villi



Bottom row: Necrosed and agglutinated villi ; and changes of thrombotic vasculopat (H&E, 400X)

Discussion

The total number of live births during the study period was 6412 with a stillbirth rate of 14.66/1000 live births, overall lesser than the na-

tional average and comparable to a study by Mustafa et al(18/1000 live births) but lower than the study by Chaudhury et al (49/1000 live births).⁽⁶⁾⁽⁷⁾ On assessing the maternal age, it was found

that 76.59% stillbirths occurred in the age group 20 to 30 years, followed by 14.89% in the > 30 years group and the least (8.50%) in the <20 years ago group. The mean maternal age was observed to be 25.64 +/- 5.46 years; however this difference in percentage of stillbirths related to maternal age was not statistically significant. ($p=0.06$). This is comparable to other studies such as by Bhattacharya et al (20-30 years) and Mustafa et al (20-35 years).^{(7) (8)} However a Western study noted an older age prominence of >35 years, probably owing to social reasons.⁽⁹⁾

Out of 94 cases, 60(63.80%) were males and 34(36.20%) were females; this was statistically significant ($p=0.003$). This was comparable to other studies.^{(7) (10)} On gross placental examination, 41.59% cases were grossly normal, while 31.91% cases were hemorrhagic and 25.50% had areas of necrosis.

Assessment of the umbilical cord is often difficult when a thorough assessment for the length and degree of coiling in particular relies on the completeness of the submitted sample, which is often not the case. Besides points of insertion and thickness, hyper coiled regions with strictures or extreme narrowing points are associated with stillbirth and is recommended to be documented.⁽¹³⁾ Although abruption is a clinical diagnosis, the presence or absence of a crater with depression of maternal cotyledons are recommended to be measured and noted; as catastrophic hemorrhage is often the cause of death.⁽¹³⁾

On histopathological examination, 40.45% cases had a normal study while 59.55% revealed abnormalities; however this was statistically insignificant. Simchen MJ et al found abnormality in 49.25%; ie. slightly lesser than our study.⁽¹¹⁾

26.59% had acute chorioamnionitis, 10.63% had infarcted chorionic villi, 13.82% had acute funisitis and 8.51% had thrombotic vasculopathy in our study.

Anitha A et al. however found a significant percentage of abnormal placentas in stillbirths, (95.29%; $p = 0.004$). They found the most common placental findings in stillbirths were abnor-

malities of the fetal villous capillaries, villitis, inflammatory lesions, and fetal circulatory disorders including terminal villous immaturity, chorionic plate acute vasculitis, acute and chronic diffuse villitis, fetal vascular thrombi in chorionic plate and avascular villi.⁽¹⁵⁾ In another study, 1/3rd of 946 cases had complete normal histology of cord, membranes and placenta while 32% cases had specific placental abnormalities such as fetal vascular occlusion, chronic histiocytic intervillitis, massive perivillous fibrin deposition and maternal vascular malperfusion.⁽¹⁶⁾

While examining cases of stillbirths, Pasztor et al found that the proportion of unexplained stillbirths remained high, with the exact cause of fetal death being determined post mortem in only 57.90% cases. The most common cause was placental insufficiency in 46.90% followed by umbilical cord complications at 25.90%. They further recommended screening for placental insufficiency as a preventive measure for the same.⁽¹²⁾

Acute diffuse (30.59%) and chronic diffuse villitis (16.47%) were significantly more in stillbirths in one study.⁽¹⁵⁾ Though gross hemorrhage maybe apparent, chronic occult hemorrhage is often evident only on histopathology by the presence of intervillous thrombi⁽¹⁴⁾ or increased nucleated RBCs in the fetal circulation and by hemisiderin laden macrophages in the membranes.⁽¹³⁾

When a history of maternal vascular malperfusion, often with a clinical history of pregnancy induced hypertension or pre eclamptic toxemia, changes of hypoxia in the placenta include accelerated villous maturity (with >33% syncytial knots at term), villous congestion and chorangiosis, and villous infarction, agglutination, distal villous hypoplasia and extravillous trophoblast proliferation.⁽¹³⁾ Changes of decidual arteriopathy in the membranes include acute atherosclerosis, fibrinoid necrosis and decidual thrombosis.⁽¹³⁾ In one study, acute funisitis was more prevalent in stillbirths, with a trend towards significance compared to live births. (10.58 vs. 2.35%; $p = 0.06$).⁽¹⁵⁾ Anitha A et al found significantly more fetal vascular thrombi in the chorionic plate (30.58%) and avascular vil-

li(24.70%) in stillbirths, Similarly, fetal vascular malperfusion arising secondary to conditions obstructing fetal blood flow, including cord lesions, hypercoaguability etc. causes thrombosis, segmental avascular villi and stream karyorrhhexis.⁽¹³⁾ Fetal vascular thrombi in the chorionic plate (30.58%) and avascular villi (24.7%) were significantly more in stillbirths than live births.⁽¹⁵⁾ In one study, importantly an additional group, representing around 20% of all cases was observed with the placenta showing some histological abnormalities of uncertain significance with majority occurring predominantly at or near term. These were labelled 'unexplained with placental lesion of unknown significance such as isolated subjective increased syncytial knots/accelerated maturation, scattered intervillous thrombi, villitis of unknown etiology, focal areas of sclerotic villi without features of fetal thrombotic vasculopathy, small infarcts and plasma cell deciduitis.⁽¹⁶⁾ The significance of these requires further research in future.

Conclusion

While stillbirths remain a still ever rising cause of perinatal and postnatal morbidity, histopathological examination of placenta is an important part of the investigative work up. Our study indicated that infectious causes still remain a leading cause in stillbirths. A proper gross and microscopic examination of placenta with documentation of all relevant findings still remains of rising relevance in addition to preventive measures to reduce stillbirths and the scope for study for the elucidation of rarer causes of stillbirths.

Limitations of the Study

Due to limited availability of facilities in our government hospital set up, causes of intrauterine fetal demise pertaining to genetic abnormalities in particular could not be evaluated.

Compliance with Ethical Standards

Funding Received: None

Conflict of Interest: The authors declare that they have no conflict of interest.

Informed Consent: was duly taken from all participants in the study.

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