ORIGINAL ARTICLE

Histopathological Study of Placenta in Intrauterine Fetal Death: A Comprehensive Study from A Tertiary Institution

Suksham Sharma, Suby Singh*

Abstract

Background:: Intra-uterine fetal death (IUFD) is the term used to describe the death of a foetus that is >24 weeks gestational age and/or >500 g in weight. The intricate process of fetal mortality involves the mother, the fetus, and the placenta; therefore these issues should be handled together **Methods:** This study was carried out in the Department of Gynaecology, GMC Jammu in collaboration with Department of Pathology w.e.f March 2021 to October 2021. A total of 114 patients with intra-uterine fetal deaths diagnosed either through ultrasound reports or on clinical examination by absence of fetal heart sound were included in the study. The study comprised placentas from all cases of intrauterine fetal deaths with gestational ages greater than 28 weeks that were received in the histopathology section of the hospital. **Results:** Majority of IUFD patients accounting for (73.7%) had (28-36) weeks of gestational age. In majority of patients, the cause of IUFD was maternal (68.4%). PIH etiology was present in (55.1%), maternal anemia was evident in 21.7%, GDM was found in 11.5% patients. Majority of patients had calcification (54.4%), followed by 37.7% with infarct finding. Perivillous fibrin was present in 65.8%, followed by syncytial knots (46.5%), intervillous haemorrhage (43.9%). **Conclusion:** The morphology of the placenta can be further studied comprehensively to learn more about pregnancy anomalies, so that an optimal strategy can be developed concerning pregnancy management and risk assessment and even preventing IUFD in subsequent pregnancies.

Keywords

Intrauterine Deaths, Placental changes in Diabetes, Placental Changes in Hypertension. Perivilloius Fibrin, Intervillous Haemorrhage.

Introduction

Intra-uterine fetal death (IUFD) is the term used to describe the death of a foetus that is >24 weeks gestational age and/or >500 g in weight.[1] Fetal death inside the womb is a painful and frequently unpredictable process. The intricate process of fetal mortality involves the mother, the foetus, and the placenta; therefore these issues should be handled together. The most easily accessible and evaluable specimen is the placenta, whose examination yields a record of pregnancy that allows for close examination of the cumulative impact of pregnancy-related events and alterations reflecting the intrauterine environment. Unfortunately, in up to two thirds of intrauterine deaths, the cause of death is listed as unknown. [2] The need for accurate cause identification is growing for medical, social, and epidemiological reasons. The placenta, an amazing versatile organ of foetal origin, plays a crucial conciliation role during pregnancy since it is so closely linked to the mother and the unborn child. Unquestionably significant, the placenta is a remarkable (and accessible) reservoir of knowledge that mirrors the uterine environment. The

Department of Gynaecology and Obstetrics, SMGS hospital, GMC, Jammu and *Department of Pathology, GMC Jammu

Correspondence to: Dr Suby Singh, H. No 7/A. Sec-D Ext ,Sainik Colony, Jammu

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results of a placental examination can be used to predict future pregnancies, provide information about the current pregnancy and its outcome, help with postpartum care, provide insight into clinical issues that emerge hours or days after delivery (such as seizures, pulmonary hypertension, or renal failure), and even be useful in medico-legal cases. In addition, numerous studies have demonstrated the necessity of a placental investigation in determining the root causes of neonatal fatalities.[3] The notion that placental inspection may not always be necessary because most newborns and placentas are healthy has fallen out of favour, and now it is encouraged even for "routine" deliveries. Given the aforementioned information, the study of placental pathology is crucial for identifying the reasons of foetal deaths and preventing their recurrence

Material and Methods

This Study was carried out in the department of Gynaecology, GMC Jammu I collaboration with Department of Pathology w.e.f from March 2021 to October 2021. A total of 114 patients with intra-uterine fetal deaths diagnosed either through ultrasound reports or on clinical examination by absence of fetal heart sound were included in the study. 114 placentas from IUFD cases delivered in the Department of Obstetrics and Gynecology served the study's major source of material. The Department of Pathology received these 114 placentas accompanied with clinical information for a comprehensive histomorphological investigation. Following criteria was strictly adopted for the inclusion of the cases:

Inclusion criteria: The present study comprised placentas from all cases of intrauterine fetal deaths with gestational ages greater than 28 weeks that were received in the histopathology section of the hospital.

Exclusion criteria: Autolysed placentas

Determination of sample size

Using GPOWER software (Version 3.0.10), it was estimated that the least number of patients required with 90% power, 5% significance level and an effect size of 0.3 is 114. Therefore we have included a total of 114 patients in our study.

Sampling design: Purposive random sampling was adopted to select 114 IUFD cases.

Placental disc examination: The placental disc was examined and sliced using the method explained by Fox H. (1964-1978).

Feta surface examination: The colour and translucency of the membranes on the fetal surface were examined. For any signs of thrombosis or calcification, vessels were examined. If overly prevalent, subchorionic fibrin was noticed. Initially, the fetal surface membranes were examined, and any nodules within or just below the amnion/chorionic layer were looked for.

Maternal surface examination: The intactness, retroplacental hematoma, calcification, infarction, and depressions of the maternal surface were evaluated. Any peculiar forms or additional lobes were observed. The entire placenta was then divided into sections measuring 0.5 to 1 cm apart. We looked for any noticeable lesions on the slices. The presence of infarct, intervillous thrombus, cysts, etc., was noticed. For a minimum of one week, the placentas were stored for fixation.

Sampling: Careful choices of representative blocks of placental tissue were made after thorough sectioning and evaluation of the placenta's sliced surface.

¢ Placental disc: From the basal plate of the placenta's core area, two blocks of the largely intact placental tissue were removed. From the periphery of two different placental lobules, two full thickness sections of the placenta were obtained, which included both the chorionic and basal plate. Any more parts from the anomalous area were also collected.

¢ Membrane: A membrane roll was taken using the Benirschke procedure for histological analysis. A section of around 10x5 cm was removed after the membranes were examined. The membrane section was then tightly rolled using forceps and placed in fixative, where it becomes rigid. Following fixation, it was cut into a jelly-roll-like structure for histological analysis. The benefit of this rolling is that it makes it possible to investigate maximum area of membranes

¢ Umbilical cord: The umbilical cord was severed from the disc at a point two to four centimetres above where it was inserted into the fetal surface.

Following fixation, all tissue fragments underwent standard paraffin tissue processing, and slices 3-5 mm thick were cut using a microtome. Hematoxylin and eosin (H&E) stain was used to routinely colour all sections. Every slide was examined under a microscope. Gross findings were verified after microscopic examination of grossly aberrant regions.

Statistical Methods: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams.

Results

In this section the results of the section will be described *Table 1*, reflects the baseline characteristics, wherein

Table 1: Baseline characteristics of study patients

Variable		Number	Percentage
Age (Years)	= 20	9	7.9
	21-25	53	46.5
	26-30	37	32.5
	> 30	15	13.2
Parity	Primigravida	61	53.5
	Multigravida	53	46.5
Mode of admission	Emergency	75	65.8
	ANC	39	34.2
Gestational age (Weeks)	28-36 Weeks	84	73.7
	37-40 Weeks	27	23.7
	> 40 Weeks	3	2.6

Table 2: Causes of IUFD among study patients

Causes of IUFD	Number	Percentage
Maternal	78	68.4
Placental	31	27.2
Fetal	5	4.4
Total	114	100

Table 3: Showing various maternal causes of IUFD

Maternal causes of IUFD	Number	Percentage
PIH	43	55.1
Anemia	17	21.8
GDM	9	11.5
Hypothyroidism	6	7.7
Rh incompatibility	2	2.6
Viral Hepatitis	1	1.3
Total	78	100

we observe that majority of IUFD patients (46.5%) were belonging to the age group of (21-25) years, followed by 32.5% patients belonging to the age group of (26-30) years, 13.2% patients were above 30 years and 7.9% patients were 20years of age. Most of the studied patients, accounting for (53.5%) were primigravida followed by (46.5%) with multigravida status. Around 65.8% patients were admitted through emergency department and 34.2% patients were admitted from ANC. Majority of IUFD patients accounting for (73.7%) had (28-36) weeks of gestational age, followed by 23.7% patients with 37-40 weeks of gestational age and only 2.6% patients had > 40 weeks gestational age

In majority of patients, the cause of IUFD was maternal (68.4%) followed by 27.2% patients with placental aetiology and 4.4% patients had fetal cause of IUFD

We observe that among the maternal causes, PIH etiology was present in (55.1%), maternal anemia was evident in 21.7%, GDM was found in 11.5% patients and rest of the maternal causes

Table 4: Showing various placental causes of IUFD

Placental causes of IUFD	Number	Percentage
Abruptio placenta	21	67.7
Oligohydramnios	6	19.4
PROM	2	6.5
Placenta Previa	2	6.5
Total	31	100

Table 5: Gross findings in placenta from cases of IUFD

Gross findings	Number	Percentage
Calcification	62	54.4
Infarct	43	37.7
Retroplacental hematoma	30	26.3

Table 6: Microscopic findings in placenta from cases of IUFD

Microscopic Findings	Number	Percentage
Perivillous fibrin	75	65.8
Syncytial knots	53	46.5
Intervillous haemorrhage	50	43.9
Cytotrophoblastisc proliferation	45	39.5
Increased vascularity	32	28.1
Fibrinoid necrosis	21	18.4
Hydropic villi	9	7.9
Villitis	7	6.1

were hypothyroidism (7.7%), Rh incompatibility (2.6%) and viral hepatitis (1.3%)

We observed that out of 31/100 placental causes of IUFD; 67.7 had abruption placenta, followed by 19.4% with oligohydramnios, PROM (6.5%), and placenta previa (6.5%) Gross findings in IUFD revealed that majority of patients had calcification (54.4%), followed by 37.7% with infarct finding and 26.3% patients with retroplacental hematoma Microscopic finding of placenta revealed that perivillous fibrin was present in 65.8%, followed by syncytial knots (46.5%), intervillous haemorrhage (43.9%), cytotrophoblastisc proliferation (39.5%), increased vascularity in (28.1%) as shown in table 6.

Discussion

In the present study on the assessment of placental pathology in cases of intrauterine fetal deaths, we have comprehensively analyzed patient's data on the basis of demographic parameters, maternal aetiology, placental aetiology of IUFD, and histopathological examination of placenta. We observed that fetal deaths were more prevalent in the age range of 21-25 years, accounting for (46.5%), followed by 32.5% of patients in the age group (26-30) years. This is compatible with the study of Mufti et al, who reported that majority of their patients were belonging to the age group of (21-30) years.[4] This is also in consonance with some previous studies conducted

by Nayak *et al.*, and Kumari *et al*.[5,6] This is due to the fact that the majority of referrals were from rural areas, where marriage is promoted at a young age. Majority of our patients were primigravida, accounting for (53.5%), followed by multigravida patients (46.5%) status. One of the risk factors for pregnancy and birthing difficulties is having a large or primigravida pregnancy. Particularly in first-time mothers, the gravida factor influences and contributes to the pregnancy and delivery processes. It is based on an immunological theory that claims that at first pregnancy happened blocking the creation of antibodies against antigens that result is imperfect and, as a consequence, can partially impede trophoblast invasion of the mother's spiral arteries and, as a result, can impair placental function. Majority of our patients were primigravida, accounting for (53.5%), followed by multigravida patients (46.5%) status. Consistent to this; Barode et al in their study also reported majority of intrauterine dead fetuses were primigravida (50.50%), followed by 46.47% with multigravida status.[7] Likewise to our study, predominance of primigravida status among such patients have also been reported by Ujwala *et al* and Sharma *et al* (2016).[8,9] Most of our studied patients accounting for (73.7%) had (28-36) weeks of gestational age, followed by 23.7% patients with 37-40 weeks of gestational age and only 2.6% patients had > 40 weeks gestational age. Much similar to this; Barode *et al* reported in their study that majority of fetuses (72.72%) with intrauterine death had 28-32 weeks gestational age, similarly, Mufti *et al* also reported that majority of their patients had 28-32 weeks gestational age followed by 33.6% cases in 33-37 gestational weeks.[4,7] There were 112 (65.8%) women who were un-booked with no antenatal visits and rest (34.2%) were booked women, which is consistent with a study by Ladhani *et al*, who reported that majority of IUFD cases (70%) were admitted through emergency department and 3o% patients were admitted from ANC.[10] In the present study; the maternal cause of IUFD was found in (68.4%) patients followed by 27.2% patients with placental aetiology and 4.4% patients had fetal cause of IUFD. Much similar to this; Barode *et al* also reported in their study that maternal aetiology was predominant in 70% of IUFD cases, followed by placental (24.25%) and fetal causes (4.04%).[7] Among the maternal causes; PIH etiology was present in (55.1%), maternal anemia was evident in 21.7%, GDM was found in 11.5% patients and rest of the maternal causes were hypothyroidism (7.7%), Rh incompatibility (2.6%) and viral hepatitis (1.3%). Likewise to our study; PIH has been identified as a major cause of IUFD in several studies.[7,11] For instance; according to a study by Barode et al PIH was present in 61.42% cases of IUFD cases, followed by maternal anemia in 25.76%.**[7]** In their investigation, Mufti et al. found that maternal hypertension disorders were strongly correlated with IUFD, followed by gestational diabetes and maternal anemia, which is comparable with the present study.4 High prevalence of severe anaemia as observed in the present study may be brought on by inadequate adherence to oral iron or folic acid therapy. However, it might be avoided with good antenatal care, and iron and folic acid supplements as advised. We observed that out of 31(27.2%) placental causes of IUFD; 67.7% had abruption placenta, followed by 19.4% with oligohydramnios, PROM (6.5%), and placenta previa (6.5%). A key contributor to serious maternal problems, placental abruption happens when the placenta separates from the uterine wall prior to delivery. A placental abruption occurs in about 1% of pregnancies, and the incidence of intrauterine foetal death (IUFD) or newborn death is reported at 20% to 40%, which is comparable with our study.[12,13] Ladhani et al in their study reported that placental abruption, PROM, and placenta praevia were the most common causes of IUFD among placental risk factors, which is similar to our study.[14] In their study, Barode *et al*. found that abruptio placenta (66.66%), oligohydramnios (16.66%), PROM and placenta previa (8.33%) were the most common findings among the placental causes of IUFD, which is in agreement with our study. In the present study; gross IUFD findings showed that majority of our patients (54.4%) had calcification, followed by 37.7% cases with infarcts and 26.3% with retroplacental hematomas. When comparing the pathological findings in IUFD placentas delivered before and after 34 weeks' gestation, a study by Amir *et al*. found that IUFD placentas delivered before 34 weeks' gestation had significantly higher rates of calcifications, infarcts, and intravascular thrombi, which is comparable with our study.[15] Contemporary to this; higher rates of calcifications, multifocal infarcts, and retroplacental hematoma (28.28%) were also noted as gross findings by Barode *et al*.[7] Much similar findings have also been reported by Patel . *et al* and Siva *et al*.[16,17] Such a meticulous gross inspection of placenta before histologic sectioning enhances the histologic interpretation through optimal area selection. In the present study; subsequent microscopic finding of placenta revealed that perivillous fibrin was present in 65.8%, followed by (46.5%) patients with syncytial knots, (43.9%) patients with intervillous haemorrhage, (39.5%) with cytotrophoblastisc proliferation, (28.1%) with increased vascularity, and 18.4% with fibroid necrosis.

Barode *et al* also reported in their study that syncytial knots were present in (44.18%), cytotrophoblastic proliferation was evident in (69.76%), and features of fibrinoid necrosis was observed in (16.27%), which is comparable with our study. [7] These microscopic placental findings are also supported by other studies.[17,18]

Conclusion

The present study has revealed that majority of IUFD cases have maternal causes, followed by placental and fetal aetiolgy. Maternal PIH and anemia were significant causes of maternal morbidity and IUFD. A vast majority of IUFD placentas reveal pathological findings that reflected placental abruption, oligohydramnios, calcification, infarct, perivillous fibrin, syncytial knots etc. Evidently placental examination makes a significant contribution in understanding the cause of intrauterine fetal mortality. The morphology of the placenta can be further studied comprehensively to learn more about pregnancy anomalies, so that an optimal strategy can be developed concerning pregnancy management and risk assessment and even preventing IUFD in subsequent pregnancies.

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Conflicts of Interest
There are no conflicts of interest.

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