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Original Research Article

A Retrospective Cohort Study to Identify the Determinants of Intrauterine Deaths

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Abstract

Background: Intrauterine foetal death (IUD) is an important indicator of pregnancy wastage and the quality of antenatal care provided to pregnant women.

AIM: The present study aimed at identifying the determinants of IUDs among pregnant women.

Material and Method: This was a single-centre, hospital-based, retrospective cohort study by enrolling a total of 1706 pregnant women. We collected data pertaining to demographic-, obstetric history, and antenatal care during the index pregnancy.

Results: Among the 1706 enrolled pregnant women there were a total of 52 cases of IUFD/stillbirth and 1654 women gave birth to a live neonate. The IUFD rates in the present study were 30.4 per 1000 births. Factors associated with IUFD included severe anaemia, pre-term labour, placental abnormalities, and umbilical abnormalities.

Conclusion: The present study is an effort to compile a profile of maternofoetal and placental causes culminating in IUD at our centre. This emphasizes the importance of proper antenatal care and identification of risk factors and their treatment.

Keywords: IUFD, IUD.

Introduction

Intrauterine foetal death (IFUD) is a distressing situation for the caregiver and a traumatic event for the family[1]. IUD definition includes antepartum deaths beyond 20 weeks of gestation or birth weight > 500gm (WHO)[2]. The American College of Obstetricians and Gynaecologists defines foetal demise as death of a foetus past 20 weeks of gestation and or weight of 500grams and above. Intrauterine foetal death may be antepartum or intrapartum. The IUFD indicate the quality of ANC services given especially the availability/access to Emergency Obstetrics Services in a country[3]. Intrauterine foetal death is a significant

contributor to perinatal mortality in developing countries although improved antenatal care, advanced techniques of perinatal diagnosis and better antepartum and intrapartum monitoring has reduced the incidence[4]. More than 3.2 million IUFD occur globally each year, yet IUFD did not get the same attention as neonatal mortality, infant mortality or under five mortalities in global health indicators, policies and programmes[5]. The incidence of Intrauterine foetal death (IUFD) incidence is 0.5–1% of all pregnancies.

Causes of IUFD vary according to gestational age[6,7] The most common causes of stillbirth worldwide are complications of childbirth, maternal infections in pregnancy, maternal disorders, foetal growth restriction and congenital abnormalities[2,3,8]. Maternal and/or foetal infections probably cause 10-25% of IUFD, most often in the early[2,3,8]. Some pathogens like parvovirus B19, CMV and toxoplasma have a clear causal relationship with IUFD, while others are associated with an increased risk of stillbirth, with strong evidence of a causal relationship absent (colonisation with urea plasma urealyticum, mycoplasma and group B streptococci)[2,3,8]. Umbilical cord accidents may cause 15% of IUFD[7,9]. Placental abruption accounts for 10 – 20% of all intrauterine foetal death but occurs in only 1% of pregnancies[10–13]. Feto-maternal haemorrhage (other than placental abruption) is probably underestimated as a cause of stillbirth but may contribute to 5% of IUFD[10–13]. About 10% of foetal deaths can be related to maternal medical illnesses such as hypertension, diabetes mellitus, systemic lupus erythematosus, chronic renal disease, thyroid disorders and cholestasis in pregnancy, but IUFD caused by these disorders have been greatly reduced in numbers the last decades thanks to better management and care.

Causes as well as risk factors differ between developing and developed countries and these differences correlate with the stillbirth rates. Fretts et al. reported that the most common causes in weeks 24-27 were infections (19%), placental abruption (14%) and foetal anomalies (14%), with 21% unexplained, while after 28 gestational weeks unexplained stillbirth was the largest group (26-40%), with foetal malnutrition (14-19%) and placental abruption (12- 18%) being frequent as well[1]. Over 90% of the IUFD placentae examined in a recent study revealed some degree of placental vascular abnormalities, regardless of gestational age. Shifts in pregnancy management, follow-up, and routine testing during recent years have changed the impact of several risk factors on IUFD cases[10–13]. However, the unexplained IUFD cases remained at a constant level throughout this period.

Targeting specific causes and specific clinical scenarios is crucial for further prevention of IUFD in high-income countries. However, the determination of a cause can be challenging, since the circumstances of the death can be complex and thus the value of a thorough investigation must be emphasized.

Aims

1. To determine the prevalence of Intrauterine Foetal Death (IUFD) among women coming for labour.
2. To identify the determinant of IUFD among women coming for labour at the study institute.
3. To determine the cause in fresh stillborn babies.

Material and Methods:

Study Design:

This was a single-centre, hospital-based, retrospective, cohort, observational, study. The present study was conducted at the Department of Obstetrics & Gynaecology, LN Medical College, Bhopal. It is a tertiary care institute. The data collection for the present study was initiated after the research protocol was approved by the

Institute's Ethical Committee on Human Research.

Study Duration:

The total duration of the study was 2 years. We analysed the medical record of all pregnant women coming for childbirth at the institute in the last two years from March 2020 to March 2022.

Inclusion Criteria:

1. All sonographically confirmed IUFD, beyond 20 weeks to full term pregnancy or died during the process of childbirth (intrauterine foetal heart sound audible but the child died during the process of birth) admitted in hospital were included in the study.

Exclusion Criteria:

1. The records of babies born before 20 weeks of gestation, foetus weighing below 500gm, and twin babies were excluded.

Sampling Methodology:

Purposive, convenience, non-random sampling methodology was employed.

Informed Consent:

Not needed. This was a secondary data analysis; no participants were interviewed for the purpose of this study. The medical records of the participants were retrieved after obtaining ethical clearance from the institute.

Data Collection:

We collected data pertaining to following variables:

1. Demographics detail
2. Obstetrics history
3. Details of the index pregnancy.
4. Details of the foetus and process of delivery

Source of Data: Medical records of hospital.

Statistical analysis plan:

The primary outcome was the prevalence of IUFD among the pregnant women giving birth at the study institute. The coded data were imported into Stata 17.1 version for analysis. For the continuous data, the mean, median, mode, standard deviation, and inter-quartile range were calculated. For discrete data, the frequency, proportion, and percentage were calculated. Continuous variables in the two comparison groups were analysed using a student's t-test. Categorical variables were analysed using chi-square (χ^2) tests. A stepwise multivariable logistics regression model was built to identify the independent risk factors for IUFD and to control for confounders. Odds ratios (OR) and 95% confidence Intervals (CI) were also calculated. A *P*-value < 0.05 was considered statistically significant.

Results:

Total of 1935 pregnant women came for the delivery at the institute during this period, but 1706 women were included in the present study- 178 women were excluded because of incomplete or improper data entries, 32 women were left out/LAMA, and remaining 19 women had multiple gestation. There were 1654 women gave birth to a live neonate and total of 52 cases had IUD/stillbirth. The IUFD rates in the present study were 30.4 per 1000 births.

Table 1 shows the mean age of the participants with and without IUFD 26.7 and 24.4 years, respectively. Pregnant women who suffered from IUFD were either very young (<20 years, 25%) or old (>30 years, 45%). Pregnant women with and without IFUD had a significant difference in their educational status (p=0.004) and occupational status (p=0.018).

Table 1: Age of the participants (n=1706)

Variable	IUFD (n=52)	Live Birth (n=1654)	P-value
<=20	13 (25.0%)	112 (6.77%)	< 0.0001
21-25	5 (9.62%)	656 (39.66%)	
26-30	10 (19.23%)	523 (%)	
31-35	17 (32.7%)	216 (%)	
>35	7 (13.5%)	147 (%)	
Mean Age	26.7	24.4	0.012
EDUCATION			
Illiterate	12(23.1%)	138(8.3%)	0.004
School level	34(65.4%)	834(50.4%)	
College level	06(11.5%)	682(41.2%)	

Table 2 shows the obstetric history of the study participants. There was no significant difference in the gravida of the women who did and did not have IUFD (p = 0.235). There was a significant difference in the proportion of women with Rh negative blood group among those who did (23.7%) and did not (9.6%) (p = 0.002). There was no significant difference among the pregnant women who did and did not have IUFD in terms of previous LSCS (p=0.72), complications in previous pregnancy (p=0.215), history of IUFD (p=0.63), history of infertility treatment (p = 0.127) and history of blood transfusion (p =0.438).

Table 2: Obstetrics History of participants (n=1706)

Variable	IUFD (n=52)	Live Birth (n=1654)	P-value
Gravida			
1	24 (46.2%)	875 (52.9%)	0.235
2	20 (38.5%)	634 (38.3%)	
>=3	8 (15.4%)	145 (8.8%)	
Rh Negative Blood Group	12 (23.7%)	158 (9.6%)	0.002
Previous LSCS	18 (34.6%)	534(32.3%)	0.72
Complication in Previous Pregnancy	14 (26.9%)	583 (35.3%)	0.215
History of Abortion	13(25.0%)	245(14.8%)	0.043
History of IUFD	7(13.5%)	187(11.3%)	0.63
History of Infertility treatment	8 (15.4%)	151(9.31%)	0.127
History of Blood Transfusion	10 (19.23%)	395 (23.9%)	0.438

Table 3 shows the features of index pregnancy among pregnant women with and without IUFD. The difference between the mean haemoglobin among the those who did (8.3 mg/dl) and did not have IUFD (9.6 mg/dl) was statistically significant (p=0.032). Further, 40.4% and 23.5% of pregnant women who did and did not have IUFD had severe anaemia (p =0.005). Moreover, 30.7% and 10.4% of pregnant women who did and did not have IUFD had blood transfusion in the present pregnancy (p =0.012). The mean gestational age of women at the time of labour of the who had IUFD was significantly lower (35.6 weeks) than those who did not had IUFD (39.8 weeks; p-value = 0.003). Only 63.8% of pregnant women who had IUFD had early registration of pregnancy in comparison to 83.8% of women gave birth to live neonate (p < 0.0001).

Table 3: Details of Index Pregnancy (n=1706)

Variable	IUFD (n=52)	Live Birth (n=1654)	P-value
Mean Hb	8.3	9.6	0.032
Hb <7.0	21 (40.4%)	389 (23.5%)	0.005
Mean Gestational age	35.6	39.8	0.003
Gestational Age < 34	21 (40.4%)	268 (16.2%)	<0.0001
Early Registration	33 (63.7%)	1386 (83.8%)	<0.001
Blood Transfusion	16 (30.7%)	173 (10.5%)	0.012

All types of antenatal morbidities like pre-eclampsia, gestational diabetes, UTI/STI, antepartum haemorrhage, amniotic and placental abnormalities were significantly higher ($p < 0.05$) among pregnant women who had IUFD in comparison to pregnant women gave birth to live neonate (Table 4). Moreover, greater than 50% of the pregnant women who suffered from IUFD have multiple antenatal morbidities.

Table 4: Complications in the Index Pregnancy (n=1706)

Variable	IUFD (n=52)	Live Birth (n=1654)	P-value
Maternal Factors			
Pre-eclampsia	12 (23.1%)	221 (13.4%)	0.045
Gestational DM	9 (17.3%)	152 (9.2%)	0.049
UTI/STI	12 (23.1%)	201 (12.1%)	0.019
APH/Vaginal bleeding	17 (32.7%)	138 (8.3%)	<0.0001
Placental Factors			
Placental abnormalities	21 (40.1%)	373 (22.5%)	0.003
Umbilical cord abnormalities	9 (17.3%)	103 (6.2%)	0.042
Amniotic fluid abnormalities	7 (13.4%)	116 (7.0%)	0.046
Foetal Abnormalities			
IUGR	9 (17.3%)	93 (5.6%)	0.039
Congenital Malformations	5 (9.6%)	0 (0.0%)	<0.0001

Discussion

The determinants of intrauterine foetal death can be categorized into maternal, foetal, and environmental factors.

1. Maternal factors that can contribute to intrauterine foetal death include[14,15]: Advanced maternal age; Pre-existing medical conditions, such as diabetes, hypertension, and kidney disease; Infections during pregnancy, such as toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and syphilis; Placental abnormalities, such as placenta previa or placental abruption; Maternal smoking, drug abuses, and alcohol consumption poor maternal nutrition and inadequate obstetric care.
2. Foetal factors that can contribute to intrauterine foetal death include[16,17]: Chromosomal abnormalities; Congenital malformations or structural abnormalities; Intrauterine growth restriction or poor foetal growth; Foetal infections, such as parvovirus B19 or listeria; Cord accidents, such as nuchal cord or cord prolapse and true knot.
3. Environmental factors associated to intrauterine foetal death include[18–22]: Exposure to environmental toxins, such as lead or mercury; Maternal stress or trauma, such as domestic violence or car accidents; Poor maternal nutrition or inadequate prenatal care; Severe weather conditions, such as extreme heat or cold; Inadequate obstetric care or delayed delivery.

In the present study, we analysed the factors associated with demography, past obstetric history, and antenatal details of the index pregnancy among the pregnant women who had intrauterine foetal death and pregnant women who gave birth to live neonate. Among the total 1706 women included in the present study: there were a total of 52 cases of IUD/stillbirth and 1654 women gave birth to a live neonate. Thus, the IUFD rates in the present study were 30.4 per 1000 births. Kanavi JV et al. (2017) reported that the incidence rate of IUFD in their study was 39 per 1000 live births[23]. Jadhav M et al., reported that IUFD rates at their institute ranged from 45·5 to 38·6 over the period of 5 years[24]. Sharma S et al., also reported that a total of 250 stillbirths amongst 6942 total births thus the incidence of stillbirths was 36/1000 births[25]. Thus, the IUFD rates were comparatively very high in the developing countries including India and low in the developed countries. One reason of higher stillbirth at our centre could be due to the selection bias due to it being a tertiary care referral centre and all major obstetric complication identified in the periphery and other centres would be referred here. The other reason could be a high number of unsupervised antenatal care due to various reasons like illiteracy, low socioeconomic status and the paucity of monitoring facilities in rural areas[26–29]. The incidence of stillbirth is higher than that reported from South India, and this could be due to the higher literacy rates, increased awareness, and better antenatal care in comparison to our area[30].

The Increased risk of foetal death is present amongst the teenage group and older women. The western studies show that increased risk is present in women over 35 years of age[1,31–33]. The strongest risk factors for IUFD in the present study were presence of multiple antenatal comorbidities. Similar to our study, Kanavi JV et al. reported that about 48 % cases of IUFD were seen among pregnant women with severe pre-eclampsia along with abruption, and HELLP syndrome[23]. In the present study, the mean gestational age of women at the time of labour had IUFD was significantly lower (35.6 weeks) than those had live births (39.8 weeks; p-value = 0.003). Kanavi JV et a., also reported that the incidence of IUFD was higher in lesser gestational age group compared to higher gestational age[23]. Further, about 43% of pregnant women who suffered from IUFD were primigravida. In comparable with Kanavi JV et al., reported 43% of cases were primipara.

In the present study, 40.4% and 23.5% of pregnant women who did and did not have IUFD had severe anaemia (p =0.005). Kanavi JV et al., reported that 48.1% of the pregnant women with IUFD had severe anaemia[23]. Moreover, 30.7% and 10.4% of pregnant women who did and did not have IUFD had blood transfusion respectively (p =0.012). In comparison Kanavi JV et al., reported 6.3% had severe anaemia needed blood transfusion[23].

IUFD is frequently ascribed to abnormalities in the umbilical cord[34–36]. In contrast to nuchal cord, which was not proven to be a statistically significant risk factor, our study indicated that real knot of cord and cord prolapse are substantial independent risk factors for IUFD. This outcome is consistent with the prevalence of cord disruptions in typical live deliveries, where only a certain threshold of disturbance results in a pathologic reaction. Histological criteria have been identified in recent investigations to differentiate between pathologic and "accidental" cord abnormalities, but more research is required to reach the conclusion. Oligohydramnios is defined as an amniotic fluid index (AFI) less than or equal to 5 cm, or a maximum vertical pocket of under 2 cm[37,38]. Oligohydramnios is associated with an increased risk for small for gestational age foetuses and stillbirth. Delivery for oligohydramnios may be indicated at 36-37 weeks gestation when no other comorbidity is identified or sooner for nonreassuring

foetal monitoring. At term, when not associated with any other risk factor, pregnancies with idiopathic oligohydramnios have similar outcomes to pregnancies with a normal amniotic fluid volume[39,40]. It is suggested that isolated oligohydramnios may be followed with antenatal testing and delivery planned after 39 weeks unless indicated for other reasons[39,40].

In the present study, there was a significant difference in the proportion of women with Rh negative blood group among those who did (23.7%) and did not (9.6%) ($p = 0.002$). Singh N et al., reported that Rh isoimmunization was reported in 1.35% of IUD in our study which was in accordance with the study by Samadi et al who reported 4.7% incidence[28]. In the present study, congenital malformation was noted among 9.6% of all women with IUFD. Singh N et al., also reported that major congenital anomalies accounted for 9.45% of cases, out of which 9 had hydrocephalous[28].

Most of the women with IUFD had multiple causes during the antenatal period. Similar to our findings, Singh N et al., and other researchers have also reported that hypertension as a leading cause of IUDs. Singh N reported that diabetes was found to be associated in 1.35% cases[28] whereas Sharma et al., reported that diabetes came out to be the major factor for IUDs [29].

Conclusion

Estimating the Intrauterine Foetal Deaths rates helps identify the contributing factors and to find strategies to prevent recurrence through effective antenatal care, early diagnosis, and management of problems. Morbidity during antenatal period, abnormalities related to placenta-, amniotic fluid-, and umbilical cord causes intrauterine foetal deaths. Clinical evaluation is recommended to assess maternal wellness, diagnose the reason of death, and prevent future pregnancy difficulties. High-risk intrapartum foetal surveillance can prevent IUFD. Our community's risk factors appear preventable. Health education should focus on antenatal care, consistent attendance, improved periconceptional environment, nutrition, and micronutrient status, notably iron and folic acid intake. High-risk cases identified and referred to higher centres may save the infant. Patient compliance reduces most unnecessary foetal losses. IUFD survivors should visit a consultant-led hospital-based antenatal clinic and have increased antenatal surveillance in their future pregnancy. Let every woman and baby count.

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