

To Study the Perinatal Outcomes in Pregnancy with Previous Stillbirth

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ABSTRACT

Background: Stillbirth is a unique challenge faced by an obstetrician, with India being the largest contributor to world's stillbirth data. Recurrent stillbirth is even more challenging for the obstetrician and family. The current study aimed at assessing the recurrence of stillbirth, causes and associated peripartum complications, to formulate a management protocol at our center.

Methodology: A retrospective cohort evaluation of the data at RMRI, Bareilly, was done from December 2020 to December 2022. All the patients with a history of previous ≥ 1 stillbirth were included. The recurrent stillbirth rate along with the parameters affecting its causation were studied.

Results: Out of a total of 2,347 pregnant females, 62 patients were identified having previous stillbirth. 17% patients had history of ≥ 2 stillbirths. Adverse perinatal outcomes was seen in 39 subjects (62%) (OR 1.7101; 95% CI 1.0183–2.8720). Hypertensive disorders of pregnancy and fetal growth restriction (FGR) were commonest medical complications associated in equal frequency (30.4%). 16% patients had early trimester abortions. Recurrence of stillbirth was observed in 8 patients, (recurrent stillbirth rate) = 12.9%. Majority of the cases were unbooked in the present pregnancy (63%). Hypertensive disorders of pregnancy was leading causative risk factor in recurrent stillbirth cases (37.5%).

Conclusions: The management of pregnancies with previous stillbirth is a unique challenge with a markedly significant incidence of occurrence of adverse perinatal outcomes and rate of recurrence of stillbirth in subsequent pregnancies. Therefore, early bookings alongside supervised help can improve perinatal outcomes in such females.

Keywords: Peri-conceptual counseling, Previous stillbirth, Recurrent stillbirth.

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INTRODUCTION

Stillbirth is one of the deadliest complications of pregnancy serving as a nightmare for obstetricians and a devastating event for the couple and family. According to WHO, a total of 2 million stillbirths take place across the globe every year with a proportion of 40% taking place during labor.¹ India is the largest contributor of stillbirth to globe having an annual incidence of 0.34 million amounting to a stillbirth rate of 13.2.²

Extremes of maternal age, hypertensive disorders of pregnancy, prematurity, fetal growth restriction (FGR) are important risk factors and predictors for stillbirth.³ The causative etiology of stillbirth is a complex interplay of multiple parameters, such as gestation age, care of antenatal services received, associated comorbid conditions, obstetric parameters, and place of birth.⁴ This intertwined interaction makes it difficult to predict subsequent stillbirth, optimize state-of-the-art intervention, and decide the ultimate level of care.

The challenge faced by a caregiver is to counsel regarding the index event and to define a strategy for the management of subsequent pregnancy in order to prevent the recurrence of stillbirth. Many times, the patients are not aware of the cause of stillbirth leading to recurrence and adversities in pregnancy outcomes in unsupervised subsequent pregnancies. Due to lack of performance of verbal autopsy, non-uniformity in records and reporting system of stillbirth in our country, leading to many times unknown status of the causation behind stillbirth to the obstetrician dealing with a pregnancy with a previous stillbirth. However, there is a bountiful of data regarding affirmation of high chances of recurrence of stillbirth seen in subsequent pregnancies, but still there is paucity of data with regards to gestational age-specific

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recurrence *per se*. The knowledge regarding this aspect can help us create gestational age-specific interventions to reduce stillbirth recurrence incidence.

Therefore, to strike a balance between the most outcome-oriented result and minimum interventions is the need of the hour.

We undertake this study to assess the rate of recurrence of stillbirth at our center, to stratify gestational age-specific risk factors for the recurrence of stillbirth and study the adverse perinatal outcomes associated with it.

Aim

To study the perinatal outcomes in pregnancy with previous stillbirth.

Objectives

To assess the incidence of recurrence of stillbirth in patients with previous stillbirth.

To study the rates of adverse perinatal outcomes in pregnancy with previous stillbirth.

To study the parameters affecting causation of recurrence of stillbirth.

Methods

A retrospective analytical study done in the Department of Obstetrics and Gynecology at Rajshree Medical Research Institute (RMRI), Bareilly, from December 2020 to December 2022.

Inclusion Criteria

All the patients with a history of previous one or more than one stillbirth were included in the study.

Exclusion Criteria

- Fetuses with congenital anomalies.
- Records with incomplete information.
- Data records of hemodynamically unstable patients and those with concomitant serious systemic infections were excluded.

The primary outcome interrogated was the recurrence of stillbirth in subsequent pregnancies of patients with previous stillbirth. The demographic and obstetrics characteristics of the study patients were analyzed.

Stillbirth was defined as an ante or intrapartum fetal death of >24 weeks of gestation or with a birth weight \geq 500 gm where gestational age was not known.

Hypertensive disorders of pregnancy included chronic hypertension, gestational hypertension, preeclampsia and eclampsia.

Hyperglycemia in pregnancy defined as pre-existing diabetes mellitus or gestational diabetes mellitus (GDM). DIPS1 was used as a single-step test to formulate a diagnosis.

Abnormal placentation included abruption placentae, placenta praevia of any grade.

Preterm birth was defined as birth at <37 weeks of gestation.

Definition of small-for-gestational age (SGA) was a birth weight below the 10th percentile for gestational age based on the gestational age-specific reference curves.

Post-term pregnancy was defined as pregnancy beyond completed 41 weeks calculated by last menstrual period or early trimester scan.

Rate of SB

The stillbirth rate (SBR) is defined as the number of babies born with no signs of life at 24 weeks or more of gestation, per 1,000 total births.

OBSTETRICAL MANAGEMENT

• Early Obstetric Intervention Studied

- Start of Ecosprin in a dose of 75 mg in 1st trimester at the time of diagnosis of pregnancy.
- Recruitment for early fetal surveillance from 26 to 28 weeks by using color doppler.
- Start of Enoxaparin or other empirical therapy in cases where pregnancy was associated with antiphospholipid antibodies (APLA).

• Expectant Management

Defined as NIL intervention until spontaneous onset of labor or crossing of expected date of delivery.

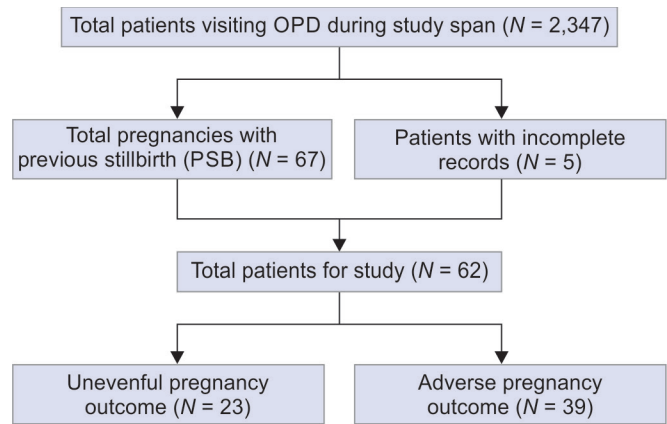


Fig. 1: Consort of the study

• Planned Delivery

Defined as elective induction of labor or elective cesarean delivery.

• Adverse Perinatal Outcome

- Stillbirth (antepartum/intrapartum fetal demise > 24 weeks gestational age or birth weight \geq 500 gm)
- Early neonatal death (within first 7 days of birth)
- Prolonged NICU Admission (> 72 hours)
- Early fetal demise/abortion
- FGR
- Preterm birth

Data analysis was done using SPSS statistics V22. Continuous variables were analyzed as mean \pm S.D, and other categorical variables were expressed as frequency, percentage, odds ratio with 95% confidence interval and were computed whenever applicable. An ethical approval from the Institute was obtained prior to the initiation of study.

RESULTS

We retrospectively analyzed the data of 2,357 deliveries at our tertiary care institute from a period of December 2020 to December 2022. A total of 67 patients were identified as having previous stillbirth. Complete records for two patients were not available and three patients did not deliver at our institute. So, a total of 62 patients were recruited for analytic study (Fig. 1).

When examined for demographic parameters, majority of the patients were in the age-group of 26–33 years (43%). Maximum number of patients had a parity of more than or equal to 2 (66%). After complete interrogation, it was found that 63% of the patients were having poor antenatal status in the form of infrequent or irregular visits (OR 1.44 95% CI (0.6767–3.0830) (Table 1). A significant finding was that out of these, 17% of the patients had two or more than two stillbirths in a previous pregnancy.

A major number presented with adverse outcomes in later duration of pregnancy, or during labor (41%), but however, a high proportion (37%) was booked at our hospital in early pregnancy. The observed incidence of adverse outcomes was lower in booked patients.

Adverse pregnancy outcomes were noted in 39 patients comprising of a proportion of 62%. About 10 patients landed in abortion (first and second trimester). Preterm birth was observed in eight patients, out of these five had preterm premature rupture of the membranes (PPROM); FGR was noted in six patients. The

recurrence of stillbirth was observed in eight patients (OR 5.6320 95% CI 2.510–12.3375). On analysis of associated medical and obstetrical factors, hypertensive disorders of pregnancy and FGR were associated in equal frequency (30.4%) patients.

Detailed obstetric outcome of the study revealed that 23 patients had uneventful pregnancy outcome. The only major observation in patients belonging to uneventful pregnancy group was the occurrence of anemia and hypothyroidism in 60.3% and 56% females, respectively (Fig. 2).

A proportion of 32% of them had moderate anemia and 11% had severe anemia. Majority of these patients had early first trimester booking (55%) and in 23% of this group, early interventions like Ecosprin and Enoxaparin were started as per their history profile.

After delivery, prolonged NICU admission was present in six patients and three early neonatal deaths were seen in this adverse perinatal outcome group (Fig. 3).

Table 1: Associated demographic and obstetric profile

	Number (n)	Percentage (%)
Age in years		
18–25	24	38
26–33	27	43
34–40	11	17
Parity		
2	21	33
>/= 3	41	66
Booking status		
Unbooked	39	63
Booked	23	37
Gestational age at admission		
1st trimester	22	35
2nd trimester	14	22
3rd trimester	26	41
Number of previous stillbirth/s		
1	52	83
>2	10	17

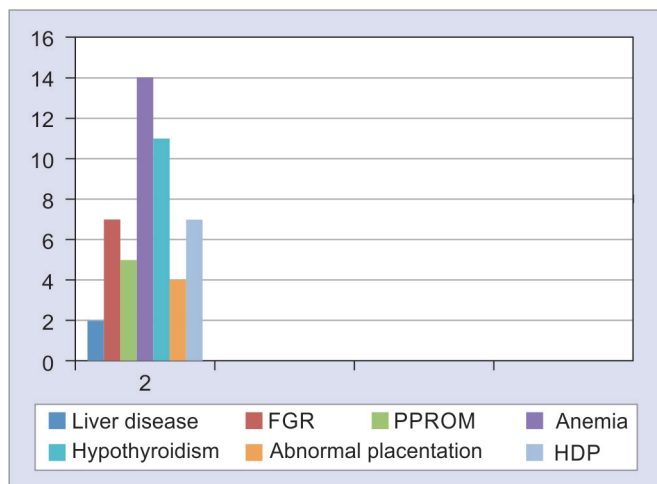


Fig. 2: Associated medical characteristics

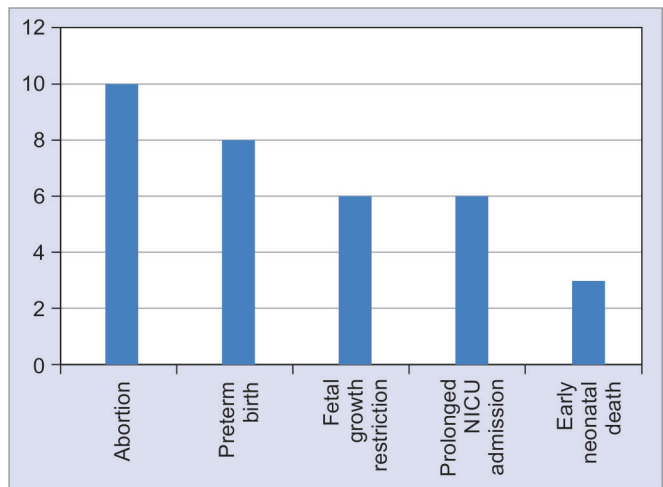


Fig. 3: Depicting the perinatal outcome

A recurrence of stillbirth was observed in eight patients. When a detailed analysis into the direct causative factors in cases with recurrent stillbirth was done, there was one case of ruptured uterus, two cases of obstructed labor with one case associated with acute fatty liver of pregnancy, one had severe growth restriction secondary to severe preeclampsia, and three very preterm births. Three patients had hypertensive disorders in pregnancy (HDP), with recurrence seen in two females (Fig. 4).

DISCUSSION

Our analysis found that having prior stillbirth predisposes to recurrence and adverse perinatal outcomes. The recurrence of stillbirth was observed in eight patients (OR 5.6320 95% CI 2.510–12.3375). Our study demonstrated high odds for recurrence in pregnancies preceded by previous stillbirth. A multicentric study was done by Kathleen Lamont⁵ and associates for comparing the prospective risk of stillbirth between women with and without a stillbirth in their previous pregnancy, it was concluded that the estimated risk of stillbirth in a subsequent pregnancy for women with stillbirth and live birth in a first pregnancy were 2.5% and 0.5%, respectively. Another large retrospective cohort study published by S Bhattacharya et al. concluded that the odds of recurrence of stillbirth in a second pregnancy were found to be 1.94 (99% CI 1.29–2.92). RSB rate in our study was found to be 12.9%. Nijkamp et al.⁶ concluded that women having previous stillbirth have a two-fold increased risk of recurrence. They observed a recurrent stillbirth rate of 8.1 per 1000 females. Such patients should be counseled during bereavement care itself and must be encouraged for periconceptional care and early pregnancy booking.

A deeper insight into the cases led the authors to conclude that almost all the cases were preventable and early fetomaternal surveillance could have benefitted and prevented the tragedies. All the cases belonged to poor socioeconomic strata and had poor antenatal care coverage. According to the global data on causative factors, half of the stillbirths were associated with intrapartum factors. Lawn JE et al.⁷ concluded that most of these deaths could be avoided with an increased access to skilled health care in time. Nijkamp et al. in their study also reported a declining risk of recurrence of stillbirth after 32 weeks, contrasting to our findings. Gestational age at recurrence was almost corresponding and coherent with previous stillbirth gestational age in 62% of our

study. Sparse data are available regarding gestational age-specific recurrence risk, which needs to be further interrogated. There is a need for further large studies for assessing gestational age stratification, as this knowledge will help in better interventional strategies (Table 2).

Adverse perinatal outcome was noted in 62% of these patients (OR 1.7101; 95% CI 1.0183–2.8720). Around 16% patients had first and second trimester abortions and 12.9% had preterm birth.

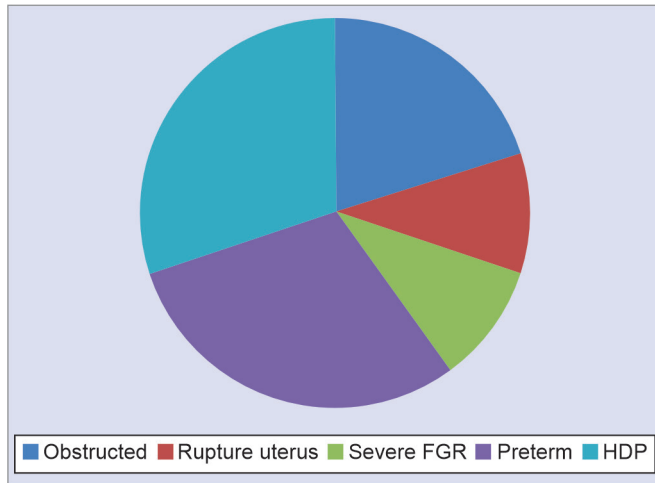


Fig. 4: Associated in patients with recurrent stillbirth

Preterm birth is the leading contributing factor to stillbirths across the globe. Recurring causes for preterm births such as hypertension, abruption and growth restriction are important etiological factors. The study by Liang et al.⁸ also noted preterm birth to be the most commonly occurring adverse outcome (16.2%) in pregnancy with previous stillbirth. At our center, there were 5% NICU admissions and out of the total NICU admissions, two required surfactant therapy. One neonatal death was subsequent to a convulsive episode in patient of GDM who got referred from adjoining primary health care (PHC). Early referrals therefore hold important role in improving perinatal care.

The noted adverse perinatal outcomes were in higher frequency in those patients who reported to us in the third trimester and had poor antenatal visits. According to the Cochrane database systematic review⁹ published in 2020, it was clearly inferred that a reduced number of antenatal care visits results in an increase in perinatal death (RR 1.14 95% CI 1.00–1.31). The data were representative of five randomized control trials, which included 56,431 women. In the present study, 63% of the patients were found to be presenting in later duration of pregnancy, or during labor (41%). The complicating associated factors have already done the damage and little can be offered to prevent such mis-incidents. The WHO proposes five visits for optimizing pregnancy outcomes based on large antenatal trial initiated in the year 2000. A secondary analysis of this WHO Antenatal Care Trial¹⁰ found an increased relative risk of fetal death of 27% between 32 and 36 weeks gestation in populations with reduced antenatal

Table 2: Descriptive analysis of cases presenting with recurrent stillbirth

Case	Gestational age at previous SB	Gestational age at present SB	Cause in previous SB	Cause in present SB
G2P1L0 with 42/3 with RFM Presented in active labor Stillborn, Male, 3.4 kg	Term	42/3 weeks	Meconium aspiration	Peripartum asphyxia, post-term
G3P1L0A1 with 37/5 weeks with obstructed labor Fetal demise <i>in utero</i> Female 2.7 kg	32/3 days	37/5 weeks	Unknown	Obstructed labor
G6P4L1A1 with 39/1 weeks with obstructed labor Transverse lie <i>In utero</i> fetal demise Female 2.6 kg	SB1 – 24 weeks SB2 – term SB3 – Term	39/1 weeks	SB1 – unknown SB2 – ?IHCP SB3 – ? IHCP	Obstructed labor IHCP was associated with comorbidity
G2P1L0 with 39 weeks with previous cesarean delivery Male 3.1 kg	37 weeks	39 weeks	Abruption placenta	Ruptured uterus
G3P2L1 at 34 weeks with IUFD Male 1.2 kg	36 weeks	34 weeks	Severe PE	Severe preeclampsia with severe FGR
G5P4L3 with 30 weeks with shock, AKI IUFD Female, 1.3 kg	34 weeks	30 weeks	PPROM	Shock Preterm AKI
G2P1L0 with 35 weeks with eclampsia Male 2.2 kg	6 months	35 weeks	APH	Preterm Eclampsia
G3P2L0 with 34 weeks with abruption placenta with IUFD Female, 1.4 kg	SB1 – 7 months SB2 – 7 months	34 weeks	SB1 – severe preeclampsia SB2 – abruption	Severe preeclampsia Preterm

APH, antepartum hemorrhage; IHCP, intra-hepatic cholestasis of pregnancy

care schedules. As per a study done by Kameswaran et al.¹¹ a five times higher risk of stillbirth occurs in emergency cases similar to Al-Kadri et al.¹² study who observed 70% risk of stillbirth in patients not receiving early antenatal care. In our study, we inferred a similar observation. Thus, in our country, a tailored number of antenatal care visits should be planned, especially in such a high-risk group. This is further supported by our observation that around 37% patients were booked at our hospital in early pregnancy and the rates of adverse incidents were lower in this group as compared with unbooked cases.

In this present study, most of the study subjects were in the age-group 26–35 years, thus indicating a high vulnerability to adverse outcomes associated with previous stillbirth in this age bracket. Extremes of age are a commonly reported risk factor for stillbirth.¹³ Our observation indicates that stillbirth has probably occurred at an earlier maternal age and thus recurrence happened in later age-group. This corroborates with the similar observation done by the author in the previous research, where teenage pregnancy was highly associated with intrauterine fetal demise (IUID).

When associated complicating factors were analyzed, hypertensive disorders of pregnancy were found to have a major causal relationship.¹⁴ Jamal et al. in their study also noted HDP to be single most dominant complicating factor. In India hypertension is the major cause for maternal morbidity and mortality. Reports around establishment of hypertension with recurrent stillbirth are sparse and patchy. More prospective analytical studies will give a robust insight on this factor.

In our analysis, we found that some or the other cause was associated with recurrent stillbirth. Fetal growth retardation and prior unexplained stillbirth are two major predictors for recurrence in future pregnancies. Nonetheless, *de novo* appearance of other causative factors, level of antenatal care, place of birth, and planned interventions can decrease the rates. Thus, evaluation of the probable cause of fetal demise is of utmost importance. Modifiable etiologies are best dealt by strategizing optimum peri-conceptual care. Our study was limited by not performing of autopsy and tissue evaluation in these cases. Therefore, further testing into such cases to identify multifactorial etiology to carry out optimum and timely interventions is warranted.

CONCLUSION

Barring the fetal losses that took place inadvertently, most of the causes that were ascertained to be associated with adverse fetomaternal outcome in our study were preventable. This impetrates our need to understand the modifiable etiology of stillbirth and to strengthen the need of optimum antenatal care in order to timely identify the risk factors. In addition, the necessity of pre-conceptual counseling in order to avoid complications and recurrence must also be emphasized. Knowledge of the gestational

age and causative etiology of previous stillbirth can serve as a good predictor, marker and guide for optimizing the outcome. Quality focused antenatal care, intrapartum care, and timely interventions can help reduce the incidence of recurrent stillbirth.

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