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Original Research Article

Study of iatrogenic preterm delivery in a tertiary center: a prospective observational study

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ABSTRACT

Background: Iatrogenic preterm delivery, also known as provider-initiated preterm birth, involves planned delivery before 37 weeks of gestation.
Methods: A prospective observational study was conducted after getting clearance from the Institutional ethics committee the study was undertaken from December 2022 to June 2024. Data will be analysed using the SPSS 26.0 software (IBM, ARMONK, NY).
Results: In the study 68% patients were primigravida .72.45% patient were between 32-37 weeks of gestation. The risk of preterm births was higher among mothers with education lower than primary level in our studies. In our study 65% women belonged to lower socio-economic group. In this study, major risk factors included hypertensive disorders in pregnancy (37 cases), PPROM (37 cases), antepartum haemorrhage (16 cases). The most common indication for induction was PPROM and that for LSCS was failure of induction and PPROM with previous scarred uterus. The caesarean section rate in our study was around 81% which included cases of failed induction of labour (20%) and only 19% delivered vaginally following induction of labour. 37.7% delivered babies weighed between 1.5-–2 kg followed by 2-2.5 kg (23.6%) and 1-1.5 kg (21.7%). Most common maternal postnatal complication were anaemia (54.2%) followed by fever (16.7%) and breast engorgement (11.5%) whereas most common neonatal complications were hypoxia (15%), followed by neonatal hyperbilirubinemia (14%) and hypoglycaemia (8%).
Conclusions: For iatrogenic preterm birth, prevention may be targeted towards modifiable factors. Research into complications of pregnancy, such as pre-eclampsia and diabetes must focus on identifying pregnancies for which it is possible to delay birth while ensuring optimal maternal and neonatal outcomes.

Keywords: Iatrogenic preterm delivery, Obstetric high-risk factors, Maternal outcomes, Hypertensive disorders, PPROM, Antepartum haemorrhage, Caesarean section rate, Neonatal complications

INTRODUCTION

Iatrogenic preterm delivery, also known as provider-initiated preterm birth, involves planned delivery before 37 weeks of gestation. This type of preterm birth accounts for nearly 50% of preterm births globally and is on the rise. This increase is often attributed to medical conditions such as preeclampsia, fetal growth restriction, and other maternal or fetal health issues that necessitate early delivery for safety reasons.[1] The causes of iatrogenic delivery, in general can be divided into four main groups: Obstetric complications (e.g. hypertensive disorders of pregnancy, placental conditions, AP (antepartum haemorrhage), Fetal causes (e.g. fetal distress, FGR (fetal growth restriction), structural malformations, Maternal medical conditions (e.g. heart disease, Pott's spine,

tuberculosis, sepsis -PPROM chorioamnionitis), non-medically indicated iatrogenic preterm delivery, for e.g. Road traffic accidents.

Based on research findings from various regions, including China and Brazil, different factors contribute to iatrogenic preterm delivery. In China, common causes include hypertensive disorders of pregnancy, placenta previa, and multiple pregnancies, while in Brazil, hypertensive disorders of pregnancy, placental abruption, and diabetes are significant contributors to iatrogenic preterm births.[2] To address these modifiable risk factors and reduce iatrogenic preterm delivery rates, strategies have been proposed. These strategies aim to target conditions such as maternal comorbidities, fetal distress, and nonmedical factors that prompt iatrogenic preterm delivery, emphasizing the importance of mitigating these risks through appropriate interventions and healthcare practices. By focusing on these identified risk factors and implementing preventive measures, healthcare providers can work towards reducing the incidence of iatrogenic preterm deliveries and improving maternal and neonatal outcomes globally.

Preterm infants have adverse long term and short-term adverse effects which includes intrapartum asphyxia, preterm delivery, RDS (respiratory distress syndrome), IVH (intraventricular haemorrhage), NEC (necrotizing enterocolitis), low APGAR, need for intubation, sepsis, seizures and neonatal death.[3] The long-term complications of FGR include impaired cognitive and neurological development, poor school performance, increased risk of childhood and adult obesity and increased risk of cardiovascular diseases, arterial hypertension and endocrine diseases like diabetes in adult life.[4,5] Hence this study was done to understand the antenatal and postnatal aspects of the patients who were at high risk for early delivery.

METHODS

Study design

Prospective observational study

Duration of the study

After getting clearance from the Institutional ethics committee the study was undertaken from December 2022 to June 2024.

Sample size

Approximately 100 patients

Inclusion criteria

100 preterm patients who were delivered by induction of labor or by LSCS before 37 weeks of gestation. Patients were divided into 3 groups- 1: less than 28weeks, 2: 28-32 weeks, 3: 32-37 weeks.

Exclusion criteria

Patient not willing to participate in the study. Stillbirth / delivery room deaths. Congenital anomalies / malformed foetuses'/Unknown due date / unconfirmed gestational age.

Place and area of study

Obstetrics and gynaecology antenatal ward/Delivery room/ postnatal ward/NICU at a tertiary centre in Mumbai.

Methods

All the patients admitted in ANC ward or labour room either referred or registered with us and who delivered before 37 weeks and satisfied all inclusion and exclusion criteria were included into the study. All patients were explained about the study and a written valid informed consent for their willingness to participate in the study was taken. Data related to various outcome variables like age, parity, socioeconomic status, the various maternal high-risk factors, indications of termination, mode of delivery (induction of labour or LSCS), the maternal and fetal outcomes of a preterm birth were noted from patient's history and case sheets and were compiled. After collecting all the information using structured proforma, the data was entered in a Microsoft office excel sheet for analysis.

Withdrawal criteria

The subject will be withdrawn from analysis if previously enrolled for the study and lost to follow up after treatment.

Statistical analysis

Data will be analysed using the SPSS 26.0 software (IBM, ARMONK, NY). All tests were two tailed and $P<0.05$ will be considered statistically significant.

Ethics

Ethical clearance was obtained from Institutional Ethics Committee (IEC) - IEC/DISS/57122 before study commencement.

RESULTS

In the study, 9% patients belonged to the extreme age groups, majority (64%) were of the age group of 21-30 years, with a mean age of 25 years 68% patients in my study were Primigravida's. All 100 patients included in the study were scored as per Kuppuswamy scoring system to define their socioeconomic status. It took into account a family's income, level of education, and the occupation of the family's primary breadwinner. This helps to evaluate

the family overall health as well as their access to resources.

Table 1: Distribution of patients according to maternal age (n=100).

Age group (years)	Frequency	Percentage
<=20	7	7
21-30	64	64
31-39	27	27
>=40	2	2

Majority (65%) of the study population belonged to the lower socio-economic class. Majority (65%) of patients in the study were referred from peripheral hospitals in Mumbai. The registered patients at our hospital (35%) followed up for regular antenatal visits in ANC OPD and were later detected to have hypertension, fetal growth restriction, placenta previa or Doppler changes.

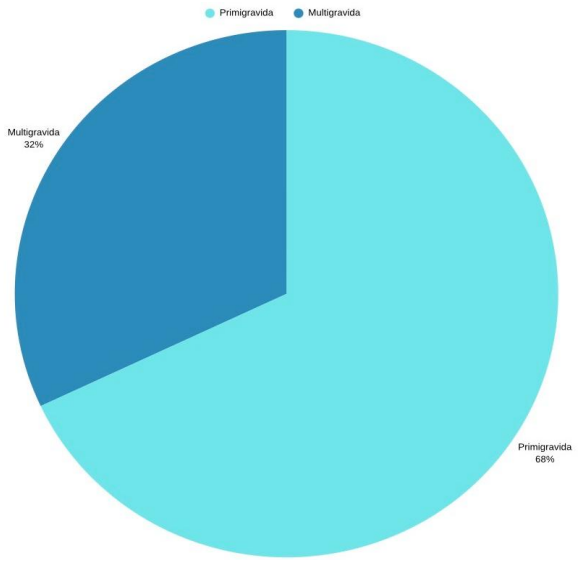

Figure 1: Distribution according to parity of patients.

Hypertension during pregnancy was the most prevalent high-risk factor. Among these (37 patients) around 31 patients had FGR foetus with or without doppler changes. Complications of severe hypertension like Impending eclampsia or severe FGR with Doppler changes were identified and diagnosed early and promptly managed.

Table 2: Distribution according to socio-economic status (modified Kuppuswamy scale) (n=100).

Socio economic status	Percentage (%)
Lower	65
Upper lower	23
Lower middle	12

Majority of cases of PPROM (37 cases) were referred from peripheral hospitals, induction of labor in these patients was awaited until steroid dose completion, wherever possible. 1 patient had uncorrected Tetralogy of Fallot, she was kept admitted in antenatal ward from 28weeks onwards and was terminated at 32 weeks in view of Doppler changes.71 patients were terminated between 32 weeks to 36 weeks and only 2 patients in the present study were delivered before 28 weeks, out of which 1 was DCDA twin gestation and other case was prolonged PPROM with chorioamnionitis. Those delivered after 32 weeks had better neonatal outcomes as compared to those delivered before. The DCDA twins delivered before 28weeks, both babies died after 6 days of life. All high-risk patients were delivered according to the clinical condition of mother either by vaginal route or LSCS. 20% of the patients induced were delivered by LSCS in view of failure of induction. The rate of LSCS 81% was significantly more than the vaginal delivery.

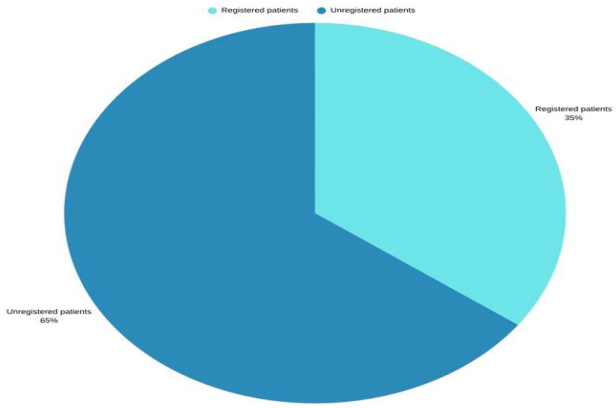

Figure 2: Distribution of patients according to ANC registration.

Most of the IUGR cases had Doppler changes in the form of changes in umbilical artery or middle cerebral artery pulsatility index or changes in the end diastolic flows. 3 Cases of severe hypertension presented as eclampsia and were managed promptly with anti-hypertensive, anti-convulsant and termination of pregnancy post stabilisation. Cases of PPROM who were directly taken for LSCS were either previously scarred uterus or prolonged PPROM with signs of chorio-amnionitis.[15]

Table 3: Distribution of patients according to the obstetric high-risk factors.

Obstetric high-risk factors	Frequency
H/O previous preterm delivery	19
Multifetal gestation	6
Pre-eclampsia without IUGR	6
Pre-eclampsia with IUGR with doppler changes	31
Gestational diabetes mellitus	13
Abruption	7
Placenta previa	9
PPROM	37
Medical disorders	2
Previous LSCS	29

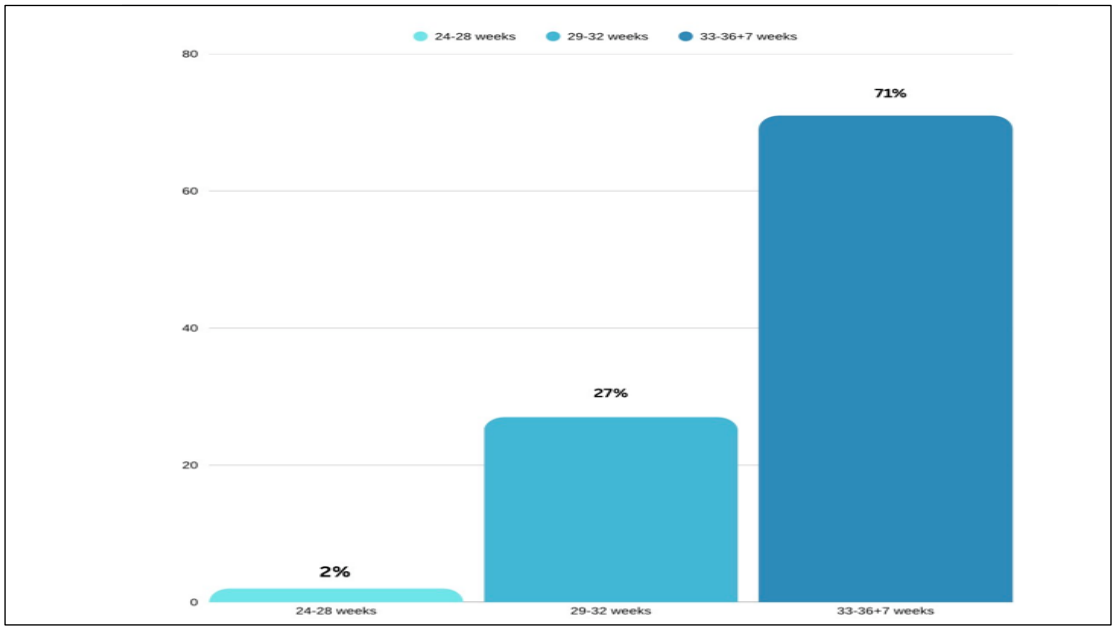

Figure 3: Distribution of patients according to the gestational age at termination.

Table 4: Distribution of patients according to the mode of delivery (n=100).

Mode of delivery	Frequency
Induction of labour followed by vaginal delivery	19
Induction of labour followed by lower segment caesarean section	20
Lower segment caesarean section	61

Table 5: Distribution of patients according to indications and mode of delivery.

Indication	Vaginal delivery (N)	LSCS (N)	Total
PPROM	15	20	35
GDM with Doppler changes	1	-	1
DCDA twins with PPROM	2	-	2
Preeclampsia with IUGR	1	-	1
IUGR with Doppler changes	-	16	16
Failure of induction	-	20	20
Antepartum haemorrhage	-	16	16
Malpresentation	-	9	9
Total	19	81	100

Table 6: Distribution of patients according to the birth weight of their babies. (n=106).

Birth weight range*	Frequency	Percentage (%)
More than 2500 grams	10	9.4
2000 - 2500 grams	25	23.6
1500 - 2000 grams	40	37.7
1000 - 1500 grams	23	21.7
Less than 1000 grams	28	7.5

*Total multifetal gestation was 6 and hence total number of live births were 106.

Table 7: Distribution of patients according to the postnatal maternal and neonatal complications.

Category	Complications type	Frequency (count)	Percentage (%)*
Maternal	Anemia	52	54.2
	Fever	16	16.7

Continued.

Category	Complications type	Frequency (count)	Percentage (%)*
	Breast engorgement	11	11.5
	Postpartum haemorrhage	8	8.3
	Wound complications	8	8.3
	Mortality- due to uncorrected tetralogy of fallot.	1	1.0
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Neonatal	Hypoxia	15	15.6
	Neonatal hyperbilirubinemia	14	14.6
	Hypoglycemia	8	8.3
	Hypothermia	6	6.3
	Meconium aspiration	6	6.3
	Septicemia	4	4.2
	Hypocalcemia	4	4.2
	Mortality	2	0.9

Patients terminated for Antepartum haemorrhage presented with bleeding placenta previa (8 cases) and abruption placenta (7 cases). Cases of twin gestation who were delivered by LSCS were previously scarred uterus or had mal-presentation.

Among the 106 live births, the vast majority (90.6%) were born with low birth weight (under 2500g), with the most common range being 1500–2000g (37.7%). While only 9.4% exceeded 2500g, nearly a third of the infants were born at very low weights under 1500g, including 7.5% who weighed less than 1000g. 57 newborn babies developed neonatal complications and were admitted to either NICU or TCU according to the severity. Majority of the babies (46) in the study group were admitted in NICU due to neonatal complications mentioned above. 15 newborn required intubations. There was 1 maternal mortality who was a known case of uncorrected Tetralogy of Fallot. Delivered at 32 weeks in view of Doppler changes by caesarean section and succumbed to post op hypovolemic and cardiogenic shock. 2 neonatal mortalities were reported. Neonatal mortality rate – 0.9 per 1000 births.

DISCUSSION

Iatrogenic preterm delivery is associated with increased risk of perinatal morbidity and mortality. The early detection of maternal risk factors and timely intervention, thus improvement in perinatal outcome should be the part of routine antenatal care of pregnancies suspected clinically to have the high-risk factors. We assessed the effect of high-risk factors of pregnancy depending on the gestational age, and found that they were the main cause associated with preterm birth. It is well-known that preterm birth is a complex syndrome and has many underlying multiple mechanisms. Our results were consistent with previous studies that preterm birth has many risk.

Demographic factors like maternal age, parity, education, socioeconomic status were evaluated in our study. In our study, 64% patients belonged to the reproductive age group and 9% belonged to the extremes of age. In a study conducted by Xi Chen et al, Zhengzhou University in China, women who underwent iatrogenic group preterm delivery belonged to older age, as women of advanced age in developed cities and have an increased risk for adverse perinatal birth and neonate outcomes, perhaps due to the high incidence of maternal complications (e.g., GDM, Preeclampsia, and Hypertension).[6] In my study 68% patients were primigravida. The study conducted by Xi Chen et al, found that nulliparous women had higher risk of preterm birth.[6] Another study conducted in Nepal by Gurung et al, also had the same findings.[7] The risk of preterm births was higher among mothers with education lower than primary level in our studies. In our study 65% women belonged to lower socio-economic group according to Kuppuswamy scale. This may be due to the fact that women hailing from lower socio-economic strata had more incidence of maternal high-risk factors and hence increased incidence of iatrogenic preterm delivery as was evident in similar studies. 35% patients were registered at my hospital and rest 65% were referred from the nearby peripheral hospitals. ANC visits should focus on improved screening of at-risk pregnant women together with the ability to treat and manage infections and provide dietary support and counselling.[9] In this study, major risk factors included hypertensive disorders in pregnancy (37 cases), PPROM (37 cases), antepartum haemorrhage (16 cases). In a similar study conducted by Lu Huang et al in USA, it was found that among all the risk factors, hypertension (2.03%), PPROM (41.8%) and placenta previa (39.18%) were observed deliveries as the independent key factors for iatrogenic preterm. In another study done by Sheng et al in Taiwan, pregnancy-related complications including gestational diabetes mellitus (3.2%), gestational hypertension (1.4%), pre-eclampsia or eclampsia (7.1%), placenta previa and abruptio placentae (11.3%), birth showed a positive correlation with preterm.[10,11]

Hypertensive disorders of pregnancy lead to poor trophoblastic invasion and thus poor nutrient supply to the foetus. Oligohydramnios is a frequent finding in pregnancies involving IUGR and is most likely secondary to decreased fetal blood volume, renal blood flow, and,

subsequently, fetal urine output. 6 of the studied patients had gestational diabetes mellitus. It has been found that chronic hyperglycaemia causes placental vascular dysfunction which leads to reduced nutrient and oxygen supply to the foetus resulting in FGR. Multiple pregnancy has long been recognized as a risk factor for preterm birth. In our study, 6 multi-fetal gestation were studied which were all twin pregnancies as triplets and more were excluded from the study. The Taiwan study showed that more than one-half of all twins is preterm. In addition, triplets and more are always born preterm.[12,13] Majority patients had more than one obstetric high-risk factors such as pre-eclampsia with IUGR with or without Doppler changes, gestational diabetes mellitus with preeclampsia with or without Doppler changes, hypertension with abruptio placentae, DCDA twins with PPROM. The study done by Lu Huang et al demonstrated high correlation between PPROM and multiple pregnancy.[10] This study was divided into 3 groups, stratified by gestational age as follows-

A comparison of gestational age at termination between Xi Chen et al's study and the current study reveals that the majority of cases occurred between 32 and 37 weeks, with the current study showing a higher concentration in this range (71% vs. 60.1%). In the 28–32-week category, Xi Chen et al reported a higher frequency at 34.7% compared to 27% in the current study. Termination at less than 28 weeks was the least common across both groups, occurring in 5.2% of cases in Xi Chen et al's research and only 2% in the current study. In the Lu Huang study, 86.83% belonged to the late preterm group and rest were early preterm birth, consistent with finding of our study.[11] The caesarean section rate in our study was around 81% which included cases of failed induction of labour (20%) and only 19% delivered vaginally following induction of labour. In the Lu Huang study, 638 preterm births were studied and a caesarean section accounted for 67.5%. The study concluded that, the rate of iatrogenic preterm birth is significantly associated with the delivery method, especially for a caesarean section. It has been demonstrated preterm birth associates with previous caesarean sections, with the higher the number of previous caesarean sections, the higher the risk of preterm birth.[10-14] By the present results, Dehaene et al found higher C-section rates in iatrogenic preterm births.[15]

In a study done by Milani et al, in Iran, aimed to evaluate the factors associated with caesarean section in preterm birth, they found that around 44% cases had previous caesarean sections.[16] In our study also 29 cases were previous scarred uterus, rest cases being PPROM, Doppler changes secondary to pre-eclampsia or IUGR, antepartum haemorrhage, mal-presentation and cases of failed induction. Administration of antenatal corticosteroid for lung maturity is important in preventing RDS (respiratory distress syndrome), PVL (periventricular leukomalacia) and severe IVH (intraventricular haemorrhage).[17] A high frequency of the use of magnesium sulphate to prevent the occurrence of eclampsia was observed in the iatrogenic group, and some initial studies have suggested that magnesium sulphate may have a protective role against IVH in preterm neonates.[18,19]

A comparison of antenatal drug use across different studies shows that dexamethasone was administered to 80% of participants in the current study, slightly lower than the 90% reported by Xi Chen et al. Regarding magnesium sulphate ($MgSO_ (4) $), the current study recorded a usage rate of 40%, while Xi Chen et al reported a significantly higher rate of 68%. Both studies show a strong clinical emphasis on dexamethasone for fetal lung maturity, though magnesium sulphate utilization for neuroprotection or preeclampsia management varied more notably between the two groups. Neonates with birth weights of less than 1,000 gram and infections have been found to have poorer head growth, more cognitive impairment, and higher rates of cerebral palsy than those who did not have infections as neonates.[20] Comparing the birth weights between the study by Xi Chen et al and the current study reveals similar results for infants weighing less than 1000 grams (7.70% and 7.50%, respectively). However, a major divergence is seen in the other categories: Xi Chen et al reported a much higher concentration of infants in the 1000–1500-gram range (68% vs. 21.70%), while the current study shows a significantly higher proportion of infants weighing more than 1500 grams (70.70% compared to 14.30%). This suggests that the current study population included a much larger percentage of relatively heavier neonates. Neonates with poor APGAR score have been found to develop complications like neonatal hyperbilirubinemia, hypoxia, hypoglycaemia, meconium aspiration, hypothermia, hypocalcaemia and septicaemia. 38.5% patients in study of Xi Chen et al developed neonatal complications, whereas in our study 57% babies developed complications. 38.5% of the babies were admitted in NICU in Xi Chen et al study whereas in our study46% babies needed NICU admission.

Limitations

In this study the area and population were from a particular tertiary care hospital in a specified geographical region and hence the findings cannot be generalized to whole population.

CONCLUSION

For iatrogenic preterm birth, prevention may be targeted towards modifiable upstream factors to ensure that women enter pregnancy well, with a normal BMI, as well as appropriate and timely surveillance of comorbidities and pregnancy complications. This requires multidisciplinary involvement extending beyond obstetric and midwifery care. Research into complications of pregnancy, such as pre-eclampsia and diabetes must focus on identifying pregnancies for which it is possible to delay birth while ensuring optimal maternal outcomes, also deciding the

timing of termination depending on the complications of the associated comorbidities. Although the incidence of preterm deliveries less than 28 weeks is not very high, the severity of neonatal morbidity and perinatal mortality in this gestational period are much higher than that of preterm babies delivered after 28 weeks. Moreover, grief and concerns regarding neonatal care and complications are much more stressful for parents and families of extremely small preterm. The results of study may be helpful for counselling patients with individualized indications for preterm birth. The current advancements in intensive care, especially in the field of neonatology, has remarkably helped to save more newborns with extremely low birth weights and earlier gestational ages. Therefore, future national population-based cohorts or worldwide data for very early and extremely small premature babies with specific maternal conditions are essential to explore maternal risk factors and long-term neonatal outcomes.

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