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PREGNANCY OUTCOME IN PRIMIGRAVIDA WITH THREATENED MISCARRIAGE - A PROSPECTIVE STUDY

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Abstract

Background: Threatened miscarriage is a common complication in early pregnancy, often associated with anxiety regarding the outcome. This study aims to evaluate the association of threatened miscarriage with adverse maternal and neonatal outcomes.

Methods: This prospective study included 96 pregnant women with threatened miscarriage (cases) and 100 pregnant women without threatened miscarriage (controls)matched for age. Data were collected on maternal age, gestational age at bleeding, bleeding amount, subchorionic hematoma, pregnancy outcomes, and neonataloutcomes. Statistical analysis was performed using the Statistical Package for the SocialSciences (SPSS) software, version 21.0. Quantitative variables were analyzed using theindependent t-test, and qualitative variables were analyzed using the Chi-square test orFisher's exact test where appropriate. A p-value of less than 0.05 was considered statistically significant.

Results: The mean age of the participants was 24.95 ± 2.92 years for cases and 24.89 ± 2.87 years for controls. In the cases group, 16.67% had spontaneous miscarriages compared to 3% in the control group (p=0.001). Subchorionic hematoma was detectedin 18.75% of cases. No significant association was found between threatened miscarriage and premature rupture of membranes (PROM), pregnancy-induced hypertension (PIH), placenta previa, or abruptio placenta. However, significant differences were observed in NICU admissions (20%

vs. 8.25%, p=0.023), low birth weight (37.50% vs. 14.43%, p=0.0004), preterm birth (30% vs. 8.25%, p=0.0002), andfetal growth restriction (FGR) (17.5% vs. 5%, p=0.023).

Conclusion: Threatened miscarriage is significantly associated with adverse maternal and neonatal outcomes, including an increased risk of spontaneous miscarriage, low birth weight, preterm delivery, NICU admissions, and FGR. Pregnancies complicated by threatened miscarriage should be considered high-risk, necessitating meticulous antenatal care, counseling, and careful planning of delivery to improve outcomes.

Keywords: Threatened miscarriage, spontaneous miscarriage, low birth weight,preterm delivery, NICU admissions, fetal growth restriction.

Introduction:

Threatened miscarriage is diagnosed when there is bloody vaginal discharge or bleeding through a closed cervix at any time during the first 20 weeks of gestation. (1sss) It may be associated with mild cramps, suprapubic pain, discomfort, or low back pain. The incidence of vaginal bleeding in the first trimester ranges from 15-25% of all pregnancies, with almosthalf resulting in pregnancy loss. (2) Approximately 20-25% of patients with threatened miscarriage experience pregnancy loss or spontaneous miscarriage. (3)

The incidence of spontaneous abortion ranges from 11-22%, with over 80% occurring within the first 12 weeks of gestation. Spontaneous abortion includes threatened, inevitable, missed, complete, and incomplete abortion. If complicated by infection, it is referred to as septic abortion.

Spontaneous abortion can result from fetal, maternal, local, and idiopathic causes. Fetal causes include chromosomal anomalies, with 50-80% attributed to aneuploidy, as well as molar pregnancy, blighted ovum, congenital defects, and multifetal pregnancy. Maternal causes encompass diseases such as diabetes mellitus, hypertension, chronic kidney disease, thyroid disorders, maternal infections, and the use of drugs such as anticonvulsants, anesthetics, and antimalarials. Other maternal causes include surgeries that induce uterine stimulation, massive blood loss leading to severe hypoxia, and luteal phase defects. Local causes involve uterine anomalies, fibroid uterus (especially submucous fibroids), cervical insufficiency, and local trauma.

The risk of adverse outcomes is greater when early bleeding is heavy rather than light (Weisset al., 2004). Maternal complications include placenta previa, placental abruption, manual removal of the placenta, cesarean delivery, and pregnancy-induced hypertension. (7)

Fetal complications encompass miscarriages, preterm rupture of membranes, preterm birth,

low birth weight, fetal growth restriction, and fetal and neonatal death. Risks for adverse outcomes increase with the severity of early bleeding. (8) The uncertainty of pregnancy outcomes often leads to stress, anxiety, and depressive symptoms in women experiencing threatened miscarriage. It is crucial to address and reassure the anxiety of these women.

The purpose of this study is to identify adverse maternal and perinatal outcomes in patients with threatened miscarriage. We included cases of primigravida and virtual primigravida women with a history of threatened miscarriage and followed them until the ultimate pregnancy outcome, including spontaneous abortion and delivery.

Materials and Methods:

This study was a prospective observational study conducted at Dept. of Obstetrics and Gynecology, IMS and SUM HOSPITAL, Bhubaneswar for a period of 2 years (2019- 2021). Convenient sampling was done and a total of 108 cases matched with controls for age group, gestational age and parity were included in the study. 12 women from cases group and 8 women from control group was lost to follow up.

Inclusion Criteria:

Primigravida and virtual primigravida with gestational age of <20 week with history ofbloody vaginal discharge where viability and singleton were confirmed on ultrasound as cases and controls matched for age, gestational age and parity attending OPD or emergency room of Department of Obstetrics and Gynaecology, IMS&SUM Hospital,Bhubaneswar during the study period and consenting to be a part of the study were included.

Exclusion Criteria:

- Multigravida
- Multiple pregnancy
- Diabetes mellitus, chronic hypertension, thyroid disease, thromboembolic diseases
- Smokers
- Uterine anomalies
- Infertility treatment
- History of recurrent pregnancy loss, trauma, or surgery

Study method:

Study groups were selected based on the inclusion and exclusion criteria. Following the informed consent process, a comprehensive patient history was obtained, and a physical examination, including a gentle sterile speculum examination, was conducted. Blood investigations and ultrasonography were also performed. Collected data encompassed

demographic details, clinical characteristics, the amount of vaginal bleeding, presence of comorbidities, blood investigation results, and ultrasonography reports for both studygroups.

Participants were followed until the ultimate pregnancy outcome, either abortion or delivery. Outcomes were documented from hospital records or through telephone follow-ups when necessary. General examinations were conducted to check for signs of pallor and record vital signs. An abdominal examination was performed to assess tenderness. Management included complete bed rest for 48 hours after bleeding cessation, folic acid supplementation, and hormonal treatment. The cases were monitored until the final pregnancy outcome, whether spontaneous abortion or delivery.

Adverse Maternal Outcomes

1. Abortion
2. Pregnancy-induced hypertension (PIH)
3. Placenta previa
4. Abruptio placentae
5. Preterm/Preterm Premature Rupture of Membranes (PROM/PPROM)
6. Mode of delivery

Adverse Neonatal Outcomes

1. Low birth weight (Birth weight <2500g)
2. Preterm birth (Gestational age at birth <37 weeks)
3. Fetal growth restriction (Estimated fetal weight <3rd percentile on Hadlock's chart)
4. NICU admissions
5. Intrauterine fetal death

Statistical Analysis

Data entry was performed using Microsoft Excel. The final analysis was conducted with the Statistical Package for the Social Sciences (SPSS) software, IBM Corporation, Chicago, USA, version 21.0. A p-value of less than 0.05 was considered statistically significant.

Quantitative variables were analyzed using the independent t-test. Qualitative variables were analyzed using the Chi-square test. In cases where any cell had an expected value of less than 5, Fisher's exact test was applied. Odds ratios with 95% confidence intervals (CI) were calculated for maternal and fetal complications.

Participants were followed until the ultimate pregnancy outcome, either abortion or delivery. Outcomes were documented from hospital records or through telephone follow-ups when necessary. General examinations were conducted to check for signs of pallor and record vital signs. An abdominal examination was performed to assess tenderness. Management included

complete bed rest for 48 hours after bleeding cessation, folic acid supplementation, and hormonal treatment. The cases were monitored until the final pregnancy outcome, whether spontaneous abortion or delivery.

Results

Table 1: Age Distribution of Cases and Control Groups

Age(years)	Cases(n=96)	Controls(n=100)	Total
20-25 years	62 (64.58%)	65 (65%)	127 (64.80%)
26-30 years	32 (33.33%)	33 (33%)	65 (33.16%)
>30 years	2 (2.08%)	2 (2%)	4 (2.04%)
Mean ± SD	24.95 ± 2.92	24.89 ± 2.87	24.92 ± 2.89
Range	20-31	20-31	20-31

Age Distribution: The study divided participants into three age groups. Both the case and control groups were matched for age. In the cases group, 64.58% were aged 20-25years, 33.33% were 26-30 years, and 2.08% were >30 years. The mean age was 24.95 ± 2.92 years. In the control group, 65% were aged 20-25 years, 33% were 26-30 years,and 2% were >30 years. The mean age was 24.89 ± 2.87 years. Most of the patients were in the 20-25 years age group, likely because most pregnancies occur at this age.

Table 2: Distribution of Gestational Age (Weeks) at Bleeding of Study Subjects

Gestational age at bleeding (weeks)	Frequency	Percentage
<10 weeks	43	44.79%
10-15 weeks	46	47.92%
>15 weeks	7	7.29%
Mean ± SD	10.09 ± 3.2	
Median (25th-75th percentile)	10(7.75-12)	
Range	5-19	

Gestational Age at Bleeding: The study subjects presented with bleeding at different gestational ages: 44.79% at <10 weeks, 47.92% at 10-15 weeks, and 7.29% at >15 weeks. Themean gestational age at bleeding was 10.09 ± 3.2 weeks.

Table 3: Distribution of Bleeding Amount of Study Subjects

Bleeding amount	Frequency	Percentage
Mild	11	11.46%
Moderate	19	19.79%
Spotting	66	68.75%
Total	96	100.00%

Amount of Bleeding: The amount of bleeding in study subjects was: 68.75% had spotting, 11.46% had mild bleeding, and 19.79% had moderate bleeding. The majority had spotting.

Table 4: Number of Abortions in Study and Controls Groups.

Abortion	**Cases (n=96)**	**Controls (n= 100)**
Number	16	3
Percentage	16.67%	3%

Number of Abortions: The number of abortions was 16.67% in the cases group and 3% in the control group.

Table 5: Distribution of Subchorionic Bleed in Study Subjects.

Subchorionic bleed	**Frequency**	**Percentage**
Absent	78	81.25%
Present	18	18.75%

Subchorionic Bleed: Out of 96 cases with threatened abortions, 18.75% had subchorionic hematoma detected on ultrasonography.

Table 6: Miscarriage in Subchorionic Hematoma (with or without)

	Subchorionic hematoma Yes (n=18)	**Subchorionic hematoma No (n=78)**	**p value**
Miscarriage	5	11	0.172
Percentage	27.7%	14.1%	

Miscarriage in Subchorionic Hematoma: Out of 18 patients with subchorionic hematoma, 5 (27.7%) had spontaneous miscarriages. Out of 78 patients without subchorionic

hematoma, 11 (14.1%) had spontaneous miscarriages. No statistical significance was observed (p=0.172)

Table 7: Comparison of Gestational Age (at Birth) in Weeks Between Cases and Controls. (Excluding Abortions And IUD)

Gestational age(at birth) in weeks	**Cases(n=78)**	**Controls(n=96)**	**P value**
<34 weeks	6 (7.69%)	1 (1.04%)	0.0005†
34 to <37 weeks	18 (23.08%)	7 (7.29%)	
>/=37 weeks	54	88	
{term}	(69.23%)	(91.67%)	
Mean ± SD	36.83 ± 2.57	38.23 ± 1.74	<.0001*
Median (25th-75th percentile)	37 (36-38)	38 (38-39)	
Range	28-41	30-42	

*** Independent t test, † Fisher's exact test**

Gestational Age at Birth: The mean gestational age at birth was 36.83 ± 2.57 weeks in the cases group and 38.23 ± 1.74 weeks in controls. Gestational age at birth was divided into <34 weeks, 34 to <37 weeks, and ≥37 weeks (term).

Table 8: Comparison of Mode of Delivery Between Cases and Controls(Excluding Abortion and IUD)

Mode of delivery	Cases(n=78)	Controls(n=96)	Total	P value
LSCS	33 (42.31%)	40 (41.67%)	73 (41.95%)	0.932‡
Vaginal delivery	45 (57.69%)	56 (58.33%)	101 (58.05%)	
Total	78 (100%)	96 (100%)	174 (100%)	

Mode of Delivery: The mode of delivery was 42.31% LSCS in the cases group and 41.67% in the control group. Vaginal delivery was 57.69% in the cases group and 58.33% in the control group. No statistically significant difference was detected regarding the mode of delivery (p=0.932).

9: Comparison of Birth Weight(kg) Between Cases and Controls.

Birth weight(kg)	Cases(n=78)	Controls(n=96)	Total
<1000 g	2 (2.56%)	0 (0%)	2 (1.15%)
1000 to <1500 g	3 (3.85%)	0 (0%)	3 (1.72%)
1500 to <2500 g	25 (32.05%)	14 (14.58%)	39 (22.41%)
2500 to 3000 g	41 (52.56%)	69 (71.88%)	110 (63.22%)
>3000 g	7 (8.97%)	13 (13.54%)	20 (11.49%)
Mean ± SD	2493.85 ± 547.6	2747.92 ± 264.37	2634.02 ± 433.48
Median (25th-75th percentile)	2650 (2300-2800)	2750 (2700-2900)	2700 (2470-2800)
Range	750-3300	2000-3200	750-3300

Birth Weight: Birth weights were divided into extremely low birth weight (<1000g), very low birth weight (1000 to <1500g), and low birth weight (1500 to <2500g).

Table 10: -Comparison of Maternal Complications Between Cases and Controls

Maternal complications	Cases(n=96)	Controls(n=100)	Total	P value	Odds ratio (95% CI)
Abortion	16 (16.67%)	3 (3%)	19 (9.69%)	0.001†	6.467(1.819 to 22.984)
PROM	8 (8.33%)	4 (4%)	12 (6.12%)	0.244†	2.182(0.635 to 7.499)
PIH	4 (4.17%)	2 (2%)	6 (3.06%)	0.438†	2.13(0.381 to 11.91)
Placenta previa	3 (3.13%)	1 (1%)	4 (2.04%)	0.361†	3.194(0.326 to 31.247)
Abruptio placenta	2 (2.08%)	1 (1%)	3 (1.53%)	0.615†	2.106(0.188 to 23.617)

Maternal Complications: Significant differences were observed in abortion rates between cases and controls (16.67% vs. 3%, p=0.001). No statistically significant differences were found for PROM, PIH, placenta previa, or abruptio placenta.

Table 11: -Comparison of Perinatal Outcomes Between Cases and Controls

Perinatal outcome	Cases(n=80)	Controls(n=97)	Total	P value	Odds ratio (95% CI)
NICU	16 (20%)	8 (8.25%)	24 (13.56%)	0.023‡	2.781(1.122 to 6.892)
Low birth weight	30 (37.50%)	14 (14.43%)	44 (24.86%)	0.0004‡	3.557(1.723 to 7.344)
Preterm	24 (30%)	8 (8.25%)	32 (18.08%)	0.0002‡	4.768(2.003 to 11.348)
FGR	14 (14.58%)	5 (5%)	19 (9.69%)	0.023‡	3.244(1.121 to 9.391)
IUD	2 (2.50%)	1 (1.03%)	3 (1.69%)	0.59†	2.462(0.219 to 27.654)

Perinatal Outcomes: Significant differences were found in NICU admissions (20% vs. 8.25%,p=0.023), low birth weight (37.50% vs. 14.43%, p=0.0004), preterm birth (30% vs. 8.25%, p=0.0002), and FGR (17.5% vs. 5%, p=0.023). No significant difference was found for intrauterine death (IUD).

Discussion

Threatened miscarriage is a common complication in early pregnancy, often associated with anxiety regarding the outcome. This study revealed that threatened miscarriage is linked with adverse maternal and neonatal outcomes. The study also evaluated the association of threatenedmiscarriage with abruptio placenta, placenta previa, pregnancy-induced hypertension (PIH), premature rupture of membranes (PROM), and intrauterine death (IUD), but found no statisticalsignificance in these associations.

In the cases group with threatened miscarriage, 16 (16.67%) experienced spontaneous miscarriage, compared to 3% in the control group. A significant association (p=0.001) was noted between threatened miscarriage and spontaneous miscarriage.

Similar studies by Dongol et al. (2011) reported a 24.2% rate of spontaneous abortion after diagnosis of threatened miscarriage.

It is hypothesized that in threatened abortion, disruption of the chorio-amniotic plane by adjacent hemorrhage may make the membrane more susceptible to rupture, or the prolonged presence of blood may act as a nidus for intrauterine infection.

Davari-Tanha et al. found statistical significance of threatened miscarriage with PPROM, 6.4% compared with 27.5%, (P < 0.001). In contrast, our study did not find a statistically significant relationship (p=0.244) between PPROM/PROM and threatened abortion. 8 (8.33%) of patientsin the cases group had PROM compared to 4 (4%) in the control group.

Our study did not find an association (p=0.438) between threatened miscarriage and PIH. Our data showed that 4 (4.17%) patients in the cases group and 2 (2%) in the control group developed PIH.

Weiss et al. (2004) found no association between vaginal bleeding in the first trimester and gestational hypertension, but they did find a low association (OR <2.0) in patients with light bleeding developing pre-eclampsia.

The incidence of placenta previa was 3 (3.13%) patients in the cases group and 1 (1%) in the control group, with no statistically significant difference found (p=0.361).

The incidence of antepartum hemorrhage of unknown location was 3% in the cases group and 0% in the control group, with no statistically significant difference found (p=0.246).

Das et al. found an increased risk for a low-lying placenta among patients with threatened abortion, but there was no difference in placental location compared to control subjects by 36 weeks of gestation. Weiss et al. (2004) found a similar association that was not statistically significant.

In our study, the incidence of abruptio placenta was 2 (2.08%) patients in the cases group and 1 (1%) patient in the control group, with no statistically significant difference found (p=0.615).This finding was supported by Ahmed et al. (2012).

Unlike our study, Weiss et al. (2004) found an increased association of placental abruption and threatened miscarriage (odds ratio, 1.6).

Davari-Tanha et al. (2008) also found that the incidence of caesarean delivery was not higher in the case group ($P < 0.455$).

The incidence of low birth weight among the cases group was 30 (37.50%) and 14 (14.43%) inthe control group. There was a statistically significant difference (p=0.0004) between cases andcontrols regarding low birth weight.

This study showed a statistically significant association (p=0.0002) of preterm birth between the cases and control groups. 24 (30%) neonates in the cases group and 8 (8.25%) neonates in the control group were delivered preterm. This finding is consistent with other studies by Wijesiriwardana et al. (2006), Hossain et al. (2007), and Sharami et al. (2012), which reportedthat bleeding in early pregnancy is associated with an increased risk of preterm delivery.

Conclusion

This study revealed that threatened miscarriage is often associated with adverse maternal and neonatal outcomes. The data showed a significantly increased risk of spontaneous miscarriage,foetal growth restriction (FGR), NICU admissions, preterm delivery, and low birth weight. It is important to consider pregnancies complicated by threatened miscarriage as high-risk. Meticulous planning of antenatal care, counselling, identification of adverse outcomes, management, and decisions regarding the place, mode, and timing of delivery can improve pregnancy outcomes

AUTHOR DECLARATION:

* Financial or Other Competing Interests: None

* Was Ethics Committee Approval obtained for this study? Yes

* Was informed consent obtained from the subjects involved in the study? Yes

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