Section: Obstetrics and Gynaecology

Original Research Article

A PROSPECTIVE OBSERVATIONAL ANALYTICAL STUDY TO COMPARE FETO-MATERNAL OUTCOME IN A MOTHER AFTER SINGLE MISCARRIAGE WITH A MOTHER HAVING A SINGLE LIVE VAGINAL DELIVERY IN A TERTIARY CARE CENTRE

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Abstract

Background: Previous spontaneous abortion may adversely affect the feto-maternal outcome of subsequent pregnancies due to common pathogenic pathways. **Materials and Methods:** A prospective, observational, and comparative study was conducted in a tertiary care centre for one and a half years, where mothers (n=131) with history of either a spontaneous idiopathic miscarriage or a term vaginal delivery were studied with regards to feto-maternal outcome from 24 weeks period of gestation upto delivery. **Results:** There was a significantly increased tendency of conceiving at short inter-pregnancy interval in case group than in controls. Mothers with history of previous spontaneous abortion were at significantly ($p<0.05$) increased risk of first trimester vaginal bleeding (suggestive of threatened abortion), PROM, preterm deliveries as compared to mothers with history of previous single live vaginal birth. Rate of caesarean section was also significantly more in cases as compared to controls. **Conclusion:** The significantly increased adverse effects in pregnancies following miscarriages must be kept in mind by treating obstetricians and these can be prevented by proper pre-conceptional counselling, antenatal monitoring and timely intervention. A proper knowledge of the possible outcomes also helps to alleviate parental mental health issues.

INTRODUCTION

Miscarriage or spontaneous abortion is defined as loss of pregnancy at less than 20 weeks gestation or with fetus weighing <500g.[1] A miscarriage may adversely affect the feto-maternal outcome,[2] and the psychological experience (anxiety and depression),[3] of parents in the next pregnancy. This study was conducted with the aim to assess and comparatively analyse the feto-maternal outcome in the second pregnancies following either a previous miscarriage or a live vaginal delivery. This will help us to formulate better pre-conceptional and antenatal management policies as well as to address parental mental health issues.

MATERIALS AND METHODS

It is a prospective, observational, comparative study conducted in a tertiary care teaching hospital for one and a half years (1st March to 31st August 2021-2022). Ethical clearance was obtained from the Institutional Ethics Committee and written informed consent was obtained from all mothers included in the study.

Second gravida mothers at 24-28 weeks of gestation, who had conceived spontaneously and attended the antenatal clinic in the tertiary care centre during the study period, with history of either a spontaneous, idiopathic miscarriage or history of a single live vaginal delivery, were included in the study and were

followed up till delivery. Informed consent was obtained from all participants of the study. Data collection was based on history, clinical examination, investigations and delivery and management methods adopted.

Mothers with known uterine anomaly, cervical incompetence, multifetal gestation, known medical disorders (likely to alter feto-maternal outcome of present pregnancy), previous surgeries (other than caesarean section), having more than one pregnancy loss, having more than one living child, having previous history of ectopic or molar gestation, addiction (alcohol or cigarette), mothers on some drug therapy and couples with known congenital disorders or mothers with a diagnosed cause of previous miscarriage were excluded from the study.

$$n = \frac{\left[\sqrt{\overline{pq}\left(1+\frac{1}{k}\right)}z_1\right] - \frac{\alpha}{z} + \sqrt{p_1q_1 + \frac{p_2q_2}{k}}z_1 - \beta}{\Delta^2}$$

Where,

where p_1, p_2 =projected true probabilities of success in two groups

$q_1 = 1 - p_1, \qquad q_2 = 1 - p_2$

$\Delta = p_2 - p_1$

$\bar{p} = \frac{p_1 + kp_2}{1+k}$

$\bar{q} = 1 - \bar{p}$

$z_{1-\beta} = 0.84$, $z_{1-\frac{\alpha}{2}} = 1.96$,

N2=k x N1

P1, p2 =proportion (incidence) of the two groups fixed, assuming level of significance at 5% and power at 80%

Based on a study by Kashanian M et al, [2]

P1 = 0.28

P2= 0.13

Thus calculating, we get,

N1=119

Assuming 10% of follow up loss. The total sample in each arm (case & control) was 131.

Based on various literature, the sociodemographic and clinical variables (likely to affect the feto-maternal outcome) like age, body mass index, residence, socio-economic status, maternal educational status and inter-pregnancy interval were compared for optimization.

The maternal outcome variables studied were hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), history of first trimester vaginal bleeding, antepartum hemorrhage (APH), prelabour rupture of membrane (PROM), mode of delivery and incidence of post-partum hemorrhage (PPH). The fetal outcome variables were presentation at delivery, gestational age at delivery [preterm <37 weeks and term ≥37 weeks], incidence of intra-uterine fetal death, APGAR score at one and five minutes, birth weight and incidence of Neonatal Intensive Care Unit (NICU) admissions.

Continuous variables were analyzed by Student's t-test or Mann- Whitney U-Test depending on distribution. Categorical data were ananlyzed by Chi-Square test or Fischer's exact test as appropriate. P<0.05 was considered statistically significant. Statistical analysis was done by MedCalc Version 18.11 (Mariakarke Belgium: MedCalc software 2012).

RESULTS

In Table 1, the socio-demographic profile and clinical history of the two study groups were compared for optimization. The number of mothers who conceived at <6 months interval after previous miscarriage were significantly more with respect to mothers having a previous live vaginal delivery [112(85.5%) vs 27(20.61%), p<0.001].

In Table 2, the feto-maternal outcome was compared between the two study groups.

A greater percentage of the mothers with history of previous spontaneous abortion, presented with history of per vagina bleeding in the first trimester of the current pregnancy as compared to mothers with previous live vaginal delivery [30 (22.90%) vs 15 (11.45%); p<0.05]. The percentage of mothers who had PROM (both at ≥37 weeks and <37 weeks) in the case group was significantly more than that in the control group [25(19.08%) and 8(6.11%) vs 8(6.11%) and 3(2.29%); p<0.05]. While the percentage of APH (due to placenta praevia or abruption or indeterminate cause) in the case group is more than that in the control group, the difference is not significant. There was no significant difference between the two study groups with respect to development of maternal co-morbidities like HDP or GDM or in the incidence of PPH.

While most babies in both the study groups were delivered at term (≥37 weeks), a significantly greater percentage of babies in the case group were delivered preterm (<37 weeks) as compared to the control group [14(10.69%) vs 5(3.82%); p<0.05]. Also, though most babies in both the groups were delivered vaginally, a significantly greater percentage of babies in the case group were delivered by caesarean section as compared to the control group [44(33.59%) vs 23(17.56%), p<0.05]. There was no significant difference in the presentation at delivery or the incidence of IUFD. Though the percentage of babies with low birth weight (<2.5 kg), with low APGAR score (<7) at both one minute and at five minutes, and with NICU admissions were more in the case group with respect to control group, the difference between the two groups were not significant.

Table 1: Distribution of Study Population According to Sociodemographic Profile and Clinical History

Parameters	Case (N=131)	Control (N=131)	P Value
Age			
<30 Years	115 (87.79%)	114 (87.02%)	0.852

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≥31 Years	16 (12.21%)	17 (12.98%)	
Mean Bmi	21.44 ± 2.044	21.43 ± 1.99	0.968
Residence			
Urban	60(45.80%)	58(44.27%)	0.804
Rural	71(54.20%)	73(55.72%)	
Socio-Economic Class			
Upper	5(3.82%)	10(7.63%)	0.274
Upper-Middle	15(11.45%)	13(9.92%)	
Lower Middle	45(34.35%)	41(31.30%)	
Upper Lower	42(32.06%)	52(39.69%)	
Lower	24(18.32%)	15(11.45%)	
Maternal Educational Status			
No Schooling	11(8.39%)	5(3.82%)	0.537
Primary (Till Class 4)	17(13%)	20(15.27%)	
Secondary (Till Class 10)	48(36.64%)	55(42%)	
Higher Secondary (Till Class 12)	32(24.42%)	30(22.9%)	
Graduate	23(17.56%)	21(16.03%)	
Inter- Pregnancy Interval			
<6 Months	112 (85.5%)	27 (20.61%)	<0.001
≥6 Months	19 (14.5%)	104 (79.39%)	

Table 2: Comparison of Feto-Maternal Outcome Parameters Among the 2 Study Population

Parameters	**Case (N=131)**	**Control (N=131)**	**P Value**
Hypertensive Disorder Of Pregnancy			
Chronic Hypertension	4(3.05%)	5(3.82%)	0.957
Gestational Hypertension	4(3.05%)	3(2.29%)	
Pre-Eclampsia	13(9.92%)	12(9.16%)	
Eclampsia	2(1.53%)	1(0.76%)	
Normotension	108(82.44%)	110(83.97%)	
Gestational Diabetes Mellitus			
No	119 (90.84%)	117 (89.31%)	0.680
Yes	12 (9.16%)	14 (10.69%)	
History Of 1st Trimester Vaginal Bleeding			
No	101 (77.10%)	116 (88.55%)	0.014
Yes	30 (22.90%)	15 (11.45%)	
Antepartum Hemorrhage			
No	114 (87.02%)	121 (92.37%)	0.564
Yes			
A) Placental Abruption	10 (7.63%)	6 (4.58%)	
B) Placenta Praevia	5 (3.82%)	3 (2.29%)	
C) Indeterminate Cause	2 (1.53%)	1 (0.76%)	
Prelabour Rupture Of Membrane			
No	98 (74.81%)	120 (91.60%)	0.001326
Prom At Term (≥37 Weeks)	25 (19.08%)	8 (6.11%)	
Pprom (At <37 Weeks)	8 (6.11%)	3 (2.29%)	
Post-Partum Hemorrhage			
No	127 (96.95%)	124 (94.66%)	0.360
Yes	4 (3.05%)	7 (5.34%)	
Presentation At Delivery			
Non-Cephalic	3 (2.29%)	4 (3.05%)	0.702
Cephalic	128 (97.71%)	127 (96.95%)	
Intra-Uterine Fetal Death			
Yes	2 (1.53%)	3 (2.29%)	0.652
No	129 (98.47%)	128 (97.71%)	
Gestational Age At Delivery			
Preterm (<37 Week	14 (10.69%)	5 (3.82%)	0.032
Term (≥37 Weeks)	117 (89.31%)	126 (96.19%)	
Mode Of Delivery			
Caeserean Section	44 (33.59%)	23 (17.56%)	0.0029
Vaginal Delivery	87 (66.41%)	108 (82.44%)	
Birth Weight			
<2.5 Kgs	8 (6.11%)	5 (3.82%)	0.393
≥2.5kgs	123 (93.11%)	126 (96.18%)	
Apgar Score			
A) At 1 Min			
<7	17 (12.98%)	16 (12.21%)	0.852
≥7	114 (87.02%)	115 (87.79%)	
B) At 5 Mins			
<7	7 (5.34%)	5 (3.82%)	0.554

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≥7	124 (94.66%)	126 (96.18%)	
Nicu Admissions			
No	105 (80.15%)	108 (82.44%)	0.635
Yes	26 (19.85%)	23 (17.56%)	

DISCUSSION

Studies have shown that pregnancies following previous single spontaneous miscarriage have adverse obstetric and perinatal outcome. This prospective observational study was conducted to comparatively analyse the feto-maternal outcome in second pregnancies following either an idiopathic spontaneous abortion or a single live vaginal delivery. First trimester vaginal bleeding may result in either a spontaneous abortion or just a threatened miscarriage which may or may not result in continuation of pregnancy. A previous miscarriage, though, increases the chance of future miscarriage, more than 70% of women with miscarriage in their first pregnancy carry a subsequent pregnancy beyond 24 weeks.[4] We chose our study population to be at more than 24 weeks period of gestation to study the feto-maternal outcomes well.

The two study population were found to be similar with respect to socio-demographic profile. However, patients conceiving at less than six months interval were significantly more in the mothers with previous miscarriage as compared to ones with previous live vaginal deliveries. This is probably due to the increased anxiety and depression following miscarriages.[5] WHO recommends a minimum gap of six months for a pregnancy after a miscarriage and a gap of at least twelve months following a live birth.[5] But there has been many recent studies including the one by Lawani LO,[6] showing that there were no significant differences with respect to adverse feto-maternal outcome in pregnancies with short and normal inter-pregnancy intervals. Hence the significant difference in interpregnancy interval among our two study population is unlikely to affect the outcome variables of our study.

Our study showed that mothers with a history of previous spontaneous idiopathic abortion were at significantly ($p<0.05$) increased risk of adverse feto-maternal outcomes like first trimester vaginal bleeding (suggestive of threatened abortion), PROM, preterm deliveries as compared to mothers with history of previous single live vaginal birth. Such adverse outcome can probably be explained by the fact that both miscarriage and placental dysfunction disorders are associated with similar pathogenesis with an imbalance in angiogenic activity (increased expression of Vascular Endothelial Growth Factor), uterine blood supply disturbance, and placental oxidative stress.[7] Genetic variance(like polymorphism in VEGF gene) is largely responsible for the endometrial control of implantation or adaptation to pregnancy.[7] This leads to the hypothesis that history of prior miscarriages might be associated with an increased risk of placental dysfunction disorders like placental abruption, preeclampsia, stillbirth, intrauterine growth restriction, preterm birth.[7] This is further supported by multiple other studies which have found statistically similar results with an increased rate of first trimester vaginal bleeding.[2,4,8,9] PROM,[8,10] preterm delivery,[8,9,10,11,12,13] pre-eclampsia,[12,13] in pregnancies following a previous loss.

While a study by Gunarsdottir,[7] found an increased risk of placental abruption, a meta-analysis by Karami,[14] found increased risk of placenta praevia in cases with previous spontaneous or induced abortions. It is probably due to damage and scarring to myometrium and endometrium of the uterus during abortions, especially in cases with surgical interference, leading to a lower uterine implantation in subsequent pregnancies. In our study, though the percentage of APH (total as well individual causes like abruption, placenta praevia and indeterminate cause) was more in the case group, the difference was not significant. A study by Dibaba B,[15] showed that women with previous history of abortion had two times increased risk of APH. However, the study by Gunnarsdottir,[7] showed that a prior single miscarriage did not increase the risk of APH while two or more prior miscarriages increased the risk.

In our study, the risk of developing HDP or GDM or incidence of PPH was not found to be significantly different in the two groups. However some studies have shown an increased risk of hypertension,[12,13] in mothers with previous history of abortion and this is probably based on the placental dysfunction hypothesis. In a recent study by Singh P,[16], it was found that antenatal complications in term of GDM, hypothyroidism and intrauterine growth restriction were more in mothers with previous abortion.

Another significant finding of our study is the significantly increased delivery rate by caesarean section in mothers with previous abortion as compared to mothers with previous vaginal delivery. Such increased rate of caesarean section has also been found in multiple studies,[2,8,9,10,12] This increased rate of caesarean section can be explained in view of the increased adverse feto-maternal outcomes in pregnancies following previous abortions.

Our study did not show any significant difference in rates of malpresentation or intra-uterine fetal death or PPH in the two groups. However some studies found an increased risk of malpresentation,[12], IUFD,[2,9] and PPH.[13]

Our study showed no significant difference in rates of low birth weight, APGAR scores and NICU admission among the case and the control group. And this finding is consistent with the study by Kashnian,[2] where neonatal complications like low birth weight, low APGAR score or gross congenital anomalies were not more in cases than in controls.

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But a study by Brown JS Jr,[17] showed that previous abortion is a significant risk factor for low birth weight and preterm delivery. Another study by Gangatkar,[18] showed significantly increased risk of low birth weight, low APGAR score at 1 and at 5 minutes and increased NICU admission rates in babies of mothers with previous history of miscarriage. As hypothesized in a study by Gunnarsdottir,[7] oxidative stress due to increased angiogenic activity and a premature onset of the maternal circulation in early placental development could result in intrauterine growth restriction and small for gestational age babies.

CONCLUSION

Thus, we conclude through our study that mothers having a history of abortion are associated with an increased risk of adverse pregnancy outcomes. Health care providers should identify and counsel women who have recent history of abortion and investigate for other risk factors. A careful pre-conceptional counselling and regular antenatal checkup will minimize the adverse feto-maternal outcome and will help to have a healthy outcome for both the mother and the baby.

However, to accept the study results as a conclusive evidence, a multicentric study and with a larger sample size is essential. Another limitation of the study is that early pregnancy complications were not evaluated here because we chose our study population beyond 24 weeks period of gestation. Psychological differences and their effect on feto-maternal outcome in pregnancies following either a previous abortion or a vaginal delivery needs elaborate subjective and objective evaluation. Also the molecular correlation in the pathogenesis of miscarriage, placental dysfunction and subsequent adverse pregnancy outcomes leave scope for future research.

Conflicts of Interest- None.

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