ORIGINAL RESEARCH

Maternal and Fetal Complications And Outcome Of Pregnancy In Patients Presenting With Threatened Abortion

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ABSTRACT

Background: This study was conducted to assess maternal and fetal complications and outcome of pregnancy in patients presenting with threatened abortion. Material and methods: Written informed consent was taken from each participating subject fulfilling the inclusion criteria after explaining the study protocol in details. A detailed history was taken including age, parity, ANC book in g status, present history including amount of vaginal bleeding, number of episodes, association with pain abdomen, aggravating/relieving factors, progesterone supplementation given, past medical, surgical and obstetric history from the patients. Detailed physical examination of each patient was done including weight, general physical examination, systemic examination, abdominal and per-vaginal examination for size of uterus, amount of vaginal bleeding, local causes of bleeding and cervical status was recorded. Data was collected from the routine investigations done for antenatal patients: Blood Group, CBC,HIV, Australia antigen, VDRL test, Glucose Challenge Test, S.TS Hand Urine routine/microscopy. Results: In 61cases with threatened abortion where pregnancy continued beyond 20weeks of gestation, premature rupture of membrane was present in 6 (9.8%) cases, manual removal ofplacenta was done in 3 (4.9%) cases, IUGR was seen in 6 (9.8%), Intrauterine Death in 1(1.6%), still birth in 2 (3.3%) and neonatal death was seen in 2 (3.3%) cases. While in 72controls, where pregnancy continued beyond 20 weeks of gestation premature rupture of membrane was done in 3 (4.2%) controls, IUGR was seen in 3 (4.2%), and still birth in 1(1.4%) controls. In trauterine Death and neonatal death was not observed in any controls. Mean APGAR score at 1 minute and 5 minutes was higher in baby born from women with threatened abortion (6.71±1.72 & 7.64±1.91 respectively) compare with baby of women without threatened abortion (7.21±0.75 & 8.04±1.25 respectively) but it was not statistically significant. Conclusion: Concluding the result of present study, first trimester bleeding can be a predicting factor for late trimester pregnancy outcome; both maternal and foetal outcomes. It is therefore necessary to consider these pregnancies as a high risk group for which antenatal care should be performed carefully. Although the cause cannot be delineated in majority of the cases of threatened abortion, but the role of oxidative stress has been proven by several studies, and the role of antioxidants in the management of threatened abortion can be further evaluated in future studies.

Keywords: maternal, fetal, pregnancy, outcomes, complications, abortion.

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INTRODUCTION

First trimester bleeding is a common complication which affects 20%-25% of all pregnancies.1 A spectrum of causes for first trimester bleed has been identified ranging from obstetric causes like Threatened Abortion, Complete Abortion, Incomplete Abortion, Missed Abortion, Gestational Trophoblastic disease, Ectopic gestation, anembryonic pregnancy, subchorionic haemorrhage; as well as non-obstetric causes such as cervicitis, vaginitis, trauma, cystitis, cervical cancer and polyp. Chromosomal abnormalities have been reported in 50-80% of first trimester spontaneous abortions, therefore the

spontaneous abortions cannot be predicted or prevented.^{2,3}About half of these first trimester bleeding will end in miscarriage within 20 weeks of gestation,^{4,5} and those women who remain pregnant have an increased risk of developing other complications later in pregnancy.⁶⁻⁹ If pregnancy continues, poor maternal and foetal outcome such as preterm delivery, preterm prelabour rupture of membranes (PPROM), placental abruption, preeclampsia and intra uterine growth restriction (IUGR) may occur. It is also known that maternal age, systemic diseases such as diabetes mellitus, hypothyroidism, infertility treatment, thrombophilia,

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maternal weight and uterine structural anomalies increase the risk of abortus imminens.10Local haemostatic factors in the uterus during implantation, decidualization, and early pregnancy, for example, tissue factor expressed in cytotrophoblasts,11 and systemic factors in the women during the ongoing pregnancies12 seem to play distinct roles in a successful pregnancy; dysfunction of any of these factors could lead to an adverse outcome¹³; for example, local formation of thrombin and soluble FMS-like tyrosine kinase-1. Both of these seem to be involved in development of placental abruption and preeclampsia.¹¹Abortion is defined as "pregnancy termination before 20 weeks of gestation or with a fetus born weighing less than 500 gm".¹⁴ It is the most common complication of pregnancy, occurring in 15-20% of ongoing pregnancies.¹ The clinical diagnosis of threatened abortion is presumed when a bloody vaginal discharge or bleeding appears through a closed cervical os during the first half of pregnancy.¹⁴ About 90-96% pregnancies with both fetal cardiac activity and vaginal bleeding at 7-11 weeks do not miscarry. The higher success rate is ssociated with bleeding at the later end of the gestational age range.¹⁵Threatened abortion has been associated with preterm labour and low birth weight (6), preeclampsia, preterm prelabour rupture of membranes (PPROM), placental abruption and intrauterine growth restriction (IUGR).¹⁶In majority of the cases of threatened miscarriage, the bleeding is of unknown origin and usually slight. On examination, cervix remains closed & uterus is appropriately sized for gestation. If the bright red blood loss continues & increases in amount, the prognosis is bad. A single bright red blood loss followed by escape of old brown altered blood usually means that the initial loss has ceased. Such dark loss may continue for several days & gradually diminishes in amount.¹⁷ Ultrasonography confirms the diagnosis. It must reveal the fetus to show signs of life (i.e., heartbeat).¹⁸ USG may show subchorionic haematoma defined as a crescent shaped echo free area between the chorionic membrane and the myometrium.¹⁹ A subchorionic haemorrhage can be present in the presence of a live gestation. In pregnancies where a hematoma is identified, the subjects should undergo repeated scans on a weekly basis until the hematoma resolves. The outcome of pregnancy can be predicted by the size of the hematoma.²⁰1st trimester ultrasound findings are also useful in calculating the period of gestation in patients who are unsure of their last menstrual period, had irregular menses prior to conception, and later in pregnancy for fetal surveillance in cases of Intrauterine Growth Restriction (IUGR). In early 1st trimester, measurement of Crown-Rump Length (CRL) and Mean Sac Diameter (MSD) approximate the gestational age (GA). Late in the first trimester, dating can be performed with the measurement of Bi-Parietal Diameter (BPD) and Head Circumference (HC) rather than CRL.²¹The outcome of ongoing pregnancies after threatened abortion is of relevance to women and obstetricians for planning antenatal care and clinical interventions in pregnancy, including additional bed rest, oral and parenteral progestogens supplementation, rigid follow up and fetal surveillance. The prognosis of threatened abortion is very unpredictable whatever method of treatment is employed either in hospital or at home. Threatened abortion is such an event during pregnancy which needs meticulous attention to fulfil the purpose. The knowledge of increased risks associated with threatened abortion may facilitate decision making regarding management and decisions regarding mode, place and timing of delivery which will inevitably improve neonatal outcome.Several studies have investigated the consequences of bleeding on the risk of complications later in the same pregnancy but there is lack of evidences from Northern part of India.The hypothesis of this study was to study the maternal and fetal complications that occur during pregnancy in a patient with threatened abortion. It also tried to evaluate possible causes of threatened abortion and role of various supportive measures which lead to favourable outcome of pregnancy.

MATERIAL AND METHODS

The study was carried out in the Department of Obstetrics & Gynaecology, Batra Hospital & Medical Research Centre, New Delhi The study population included 75 cases with threatened abortion and 75 control patients. Every case was matched with one control of same age group and parity. Inclusion criteria for the present study included patients having a history of threatened abortion, i.e. 1 or more episode of vaginal spotting or bleeding before 20 weeks of gestation for study group and No episode of vaginal bleeding or spotting before 20 weeks of gestation for control group. Written informed consent was taken from each participating subject fulfilling the inclusion criteria after explaining the study protocol in details. A detailed history was taken including age, parity, ANC book in gstatus, present history including amount of vaginal bleeding, number of episodes, association with pain abdomen, aggravating /relieving factors, progesterone supplementation given, past medical, surgical and obstetric history from the patients. Detailed physical examination of each patient was done including weight, general physical examination, systemic examination, abdominal and peraginal examination for size of uterus, amount of vaginal bleeding, local causes of bleeding and cervical status was recorded. Data was collected from the routine investigations done for antenatal patients: Blood group, CBC, HIV, Australia antigen, VDRL test, Glucose Challenge Test, S.TSH and Urine routine/ microscopy. Data was collected from ultrasound findings in 1st trimester for confirmation of site and number of embryos, foetal viability, gestational age, subchorionic haemorrhage, cervical status; as well as subsequent ultrasounds done in

pregnancy for assessment of foetal growth, placental status, amniotic fluid volume and Doppler abnormalities.

METHOD

2groups of subjects were selected

STUDY GROUP

This group include patients with an occurrence of threatened abortion(history of vaginal bleeding before 20weeks of gestation with a viable foetus).

CONTROL GROUP

An equal number of antenatal patients of similar age and parity were selected who did not have any occurrence of threatened abortion. The cases and controls were followed up regularly in antenatal clinics and in the wards. All patients were followed during labour and early postnatal period till time of discharge, in collaboration with the neonatologist. The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated usingSPSS-PC-17 version. Quantitative data was expressed in mean, standard deviation and difference between two comparable groups were tested by student" s t-test (unpaired) or Mann Whitney "U" test. Three or more group"s mean was analyzed using one-way ANOVA, while qualitative data were expressed in percentage. Statistical differences between the proportions were tested by chi square test or Fisher" s exact test. "P" value less than 0.05 was considered statistically significant.

RESULTS

Table 1: Maternal complications in study subjects

| Maternal complications | Cases(N=61) | | Contr | P value | |
|------------------------|-------------|------|-------|---------|------|
| | No. | % | No. | % | |
| APH | 10 | 16.4 | 5 | 6.9 | 0.08 |
| PIH | 8 | 13.1 | 4 | 5.6 | 0.14 |
| PPH | 7 | 11.5 | 4 | 5.6 | 0.34 |
| Abruptio placentae | 5 | 8.2 | 2 | 2.8 | 0.24 |
| Placenta Previa | 5 | 8.2 | 1 | 1.4 | 0.09 |
| | | | | | |

For cases n was reduced to 61 as 14 were aborted while for controls n was reduced to 72 due to 3 abortions. In 61 cases with threatened abortion where pregnancy continued beyond 20 weeks of gestation, the maternal complications were APH in 10 (16.4%) cases, placenta previa in 5 (8.2%) cases, placental abruption in 5 (8.2%) cases, PIH in 8 (13.1%) cases and PPH wasseen in 7 (11.5%) of cases. While in 72 controls, where pregnancy continued beyond 20 weeks of gestation, the maternal complications were APH in 5 (6.9%) cases, placenta previa in 1 (1.4%) cases, placental abruption in 2 (2.8%) cases, PIH in 4 (5.6%) cases and PPH was seen in 5 (5.6%) of cases. Although maternal complications were more common in threatened abortion group but difference was not found to be statistically significant.

| Maternal complications | NoSCH (n=42) | | SCH pres | | |
|------------------------|--------------|-----|----------|------|---------|
| | No. | % | No. | % | P value |
| Abortion | 4 | 9.5 | 10 | 30.3 | 0.03 |
| APH | 2 | 4.8 | 8 | 24.2 | 0.01 |
| PIH | 2 | 4.8 | 6 | 18.2 | 0.12 |
| PPH | 3 | 7.1 | 4 | 12.1 | 0.69 |
| Abruptio placentae | 2 | 4.8 | 3 | 9.1 | 0.64 |
| Placenta Previa | 1 | 2.4 | 4 | 12.1 | 0.16 |

Table 2: Association of Maternal complications with SCH

Pregnancy was aborted in 10 (30.3%) women with threatened abortion in which subchorionic hematoma was seen on ultrasonography while pregnancy was aborted in 4 (9.5%) women without subchorionic hematoma. Other maternal complications like APH (n=8; 24.2%), Pregnancy induced hypertension (n=6; 18.2%), PPH (n=4; 12.1%) abruption placentae (n=3; 9.1%) and placenta previa (n=4; 12.1%) were more commonly seen in women with subchorionic hematoma compared to without subchorionic hematoma.

Table 3: Gestational age at the time of delivery in study subjects

| | Cases(n=61) | Controls(n=72) | P value |
|--|------------------|------------------|-----------|
| Period of Gestation in weeks at the time of delivery(Mean ±SD) | 36.45 ± 1.97 | 38.13±2.08 | < 0.01 |
| In the current study, the mean gestational age of patients at time of deli | verv in cases | was 36.45 + 1.97 | weeks and |

 38.13 ± 2.08 weeks in control group. This difference between the groups was statistically significant (p <0.01).

Table 4: Mode of delivery in study subjects

| Cases(n=61) | | Contr | | |
|-------------|--------------------------|---|---|--|
| No. | % | No. | % | P value |
| 37 | 60.7 | 48 | 66.7 | 0.47 |
| 24 | 39.3 | 24 | 33.3 | |
| | Cases No. 37 24 | Cases(n=61) No. % 37 60.7 24 39.3 | Cases(n=61) Contr No. % No. 37 60.7 48 24 39.3 24 | Cases(n=61) Controls(n=72) No. % No. % 37 60.7 48 66.7 24 39.3 24 33.3 |

Among the 61 patients in whom pregnancy continued beyond 20 weeks, 60.7% of the patients had vaginal delivery and 39.3% had caesarean section while in among 72 controls,48 (66.7%) had vaginal delivery and 24 (33.1%) had caesarean section.

Table 5: Type of delivery in study subjects

| Type of delivery | Cases | (n=61) | Contr | ols(n=72) | |
|------------------|-------|-----------------|-------|-----------|---------|
| | No. | % | No. | % | P value |
| Term | 44 | 72.1 | 63 | 87.5 | 0.02 |
| Preterm | 17 | 27.9 | 9 | 12.5 | |

Women with threatened miscarriage had a significantly increased risk of preterm labor (less 37 weeks of gestation) compared with the control group (27.9% vs 12.5%, p=0.02).

Table 6: Birth weight of baby in study subjects

| | Cases(n=61) | Controls(n=72) | P value |
|--|----------------|----------------|---------|
| Birth weight of baby in grams(Mean±SD) | 2476.75±386.35 | 2803.60±366.43 | < 0.01 |

Women with threatened miscarriage had significantly small babies with a mean birth weight(2476.75 ± 386.35 vs 2803.60 ± 366.43 gm, p <0.01).

Table 7: Low birth weight in study subjects

| Birth weight | Cases(n=61) | | Contr | | |
|--------------|-------------|------|-------|------|---------|
| | No. | % | No. | % | P value |
| <2.5kg | 24 | 39.3 | 9 | 12.5 | < 0.001 |
| ≥2.5 kgs | 37 | 60.7 | 63 | 87.5 | |

Women with threatened miscarriage had significantly small babies weighing less than 2.5 kgcompared with the control group (39.3% compared to 12.5% respectively).

Table 8: Perinatal outcome in study subjects

| Perinatal outcome | Cases(n=61) | | Controls(n=72) | | P value |
|----------------------------|-------------|-----|----------------|-----|---------|
| | No. | % | No. | % | |
| PROM | 6 | 9.8 | 3 | 4.2 | 0.30 |
| Manual removal of placenta | 3 | 4.9 | 0 | 0.0 | 0.09 |
| IUGR | 6 | 9.8 | 3 | 4.2 | 0.30 |
| IUD | 1 | 1.6 | 0 | 0.0 | 0.45 |
| Still birth | 2 | 3.3 | 1 | 1.4 | 0.59 |
| Neonatal death | 2 | 3.3 | 0 | 0.0 | 0.20 |

In 61 cases with threatened abortion where pregnancy continued beyond 20 weeks of gestation, premature rupture of membrane was done in 6 (9.8%) cases, manual removal of placenta was done in 3 (4.9%) cases, IUGR was seen in 6 (9.8%), Intrauterine Death in 1 (1.6%), still birth in 2 (3.3%) and neonatal death was seen in 2 (3.3%) cases. While in 72 controls, where pregnancy continued beyond 20 weeks of gestation premature rupture of membrane was done in 3 (4.2%) controls, IUGR was seen in 3 (4.2%), and still birth in 1 (1.4%) controls. Intrauterine Death and neonatal death was not observed in any controls.

Table 9: APGAR score in study subjects

| APGAR score | Cases | Controls | P value |
|---------------------|-----------|-----------|---------|
| At 1minute(Mean±SD) | 6.71±1.72 | 7.21±0.75 | 0.07 |
| At 5 minutes | 7.64±1.91 | 8.04±1.25 | 0.14 |

Mean APGAR score at 1 minute and 5 minutes was higher in baby born from women with threatened abortion $(6.71\pm1.72 \& 7.64\pm1.91 \text{ respectively})$ compare with baby of women without threatened abortion $(7.21\pm0.75 \& 8.04\pm1.25 \text{ respectively})$ but it was not statistically significant.

| NICU admission | Cases(n=58) | | Contr | | | | | |
|----------------|-------------|------|-------|------|---------|--|--|--|
| | No. | % | No. | % | P value | | | |
| Yes | 12 | 20.7 | 7 | 9.9 | 0.13 | | | |
| No | 46 | 79.3 | 64 | 90.1 | | | | |
| | | | | | | | | |

Table10: NICU admission in study subjects

Out of 58 cases, NICU admission was required in 12 (20.7%) newborn while NICUadmission was required in 7 (9.9%) controls (p=0.13).

DISCUSSION

The present study entitled "Maternal and fetal complications and outcome of pregnancy in patients presenting with threatened abortion" was a hospital based Prospective cohort study carried out in the Department of Obstetrics & Gynaecology, Batra Hospital & MedicalResearch Centre, New Delhi over a period of 8 months from October 2018 to May 2019. The study population included 75 cases with threatened abortion and 75 control patients. The study was done to evaluate the maternal and fetal complications and pregnancy outcome in patients presenting with threatened abortion. Pregnancy related bleeding is a clinical challenge and is associated with significant maternal and fetal morbidity. The probability of abortion and adverse pregnancy outcome increases as the amount and duration of bleeding increases especially when accompanied with lower abdominal pain.22 Firsttrimester bleeding is not only associated with miscarriage but also with a higher rate of pregnancy complications. First trimester bleeding is often a sign of threatened abortion and as such worrisome for both patient and doctor. If on ultrasound a viable fetus is observed and there is a blood collection or clot around the fetal sac, it seems worthwhile to advice the patient to take bed rest; however, there is no evidence that any conservative or medical management is beneficial. Neither progesterone nor HCG injections have demonstrated to be beneficial in improving pregnancy outcome.23 In a study by Snell et al, it was demonstrated that vaginal bleeding occurs among 15-25% of pregnancies and half of them continue their pregnancy.24,25 Three major reasons for first trimester bleeding are spontaneous abortion, ectopic pregnancy and trophoblastic diseases in pregnancy. In a study by Dogra et al. it is reported that the most common causes for first trimester bleeding are abortion and ectopic pregnancy, and there were observable genetic disorders in more than 50% of spontaneous abortions.26 Both group were almost similar in term of age distribution. 30 (40%) patients were between the age group of 26-30 years in cases and 28 (37.4%) in controls while 24 (32.0%) subjects were between the age group of 21-25 years in cases and 22 (29.3%) in controls. 22 subjects in both the groups were >35 years of age. The mean maternal ages for the threatenedmiscarriage and the control groups were 25.45±4.32 and 26.11±4.93 years respectively. In the study by Amirkhani Z et al27 53% patients were in the age group between 25-34 years of age. There was no significant difference within age

distribution of the groups (p=0.34). The mean BMI for the threatened miscarriage and the control groups was 22.46±2.87 and 23.12±2.88 kg/m2 respectively. There was no significant difference within BMI distribution of the groups (p=0.16). 34 (45.3%) subjects in cases were primigravida while 26 (34.7%) subjects in controls were primigravida. No significant difference was observed in gravida distribution. This data was consistent with the existing literature available.28-30 Similar to our study, Agarwal S et al31 reported mean age in study and controls group as 23.85±3.48 years and 23.78±3.07 years while mean BMI in their study was 20.67 \pm 1.26 kg/m2 in cases and 20.53±1.43 kg/m2 in controls which is similar to our study. In contrast to our study, Yakıştıran B et al10 reported higher maternal age in threatened abortion group (33.5±5.4 years) compare to controls (28.8±5.2 years). Mean gravidae in their study was also higher in threatened abortion group (2.1 ± 1.2) compare to control group (1.9 ± 1.1) . In study by Kamble PD et al23, 64% patients who came with first trimester bleeding were primigravidas and 36% were multigravidas. Amirkhani Z et al27 reported that 56.7% patients who presented with firsttrimester bleeding were primigravidas and 43.3% were multigravidas. In the women who continued their pregnancy, 32.9% were gravida 1, 60.7% were gravid 2 and 3 and 7% were gravida >3. Among 75 women with threatened abortion, history of abortion in previous pregnancy was present in 16 (21.3%) subjects while in 75 controls, history of abortion was reported by 8 (10.7%) women. Out of 16 women who gave history of abortion in previous pregnancy, 6 (37.5%) gave history of 1 abortion while 8 (50.0%) gave history of 3 abortions while in 8 controls with history of abortion, 5 reported 1 abortion in previous pregnancy, and only 1 (12.5%) reported 3 previous abortions. In the study by Patel S et al22, 40% patients of first trimester bleeding had a history of previous spontaneous/induced abortion. Out of those 40 patients, 16 (40%) pregnancies terminated before 20 weeks and 24 (60%) continued beyond 20 weeks. Out of 75 women with threatened abortion, progesterone support was given in 61 (81.3%) cases while among 75 controls, progesterone support was given in 21 (28.0%) subjects. Out of 61 women with threatened abortion in which progesterone support was provided pregnancy was continued in 52 (85.2%) women while 9 (14.8%)were aborted spontaneously.In 14 cases without progesterone support, pregnancy was continued in 9 (64.3%) women while 5 (35.7%) were aborted. There was no significant difference in results with different types of progestogens and their mode of administration, which is supported by studies suggesting all types of progesterones have similar efficacy in supporting pregnancy.

In our study the overall adverse pregnancy outcomes were higher in cases than the control group. Several studies have reported an association between first trimester bleeding and abnormal pregnancy outcome, including preterm deliveries, fetal growth restriction, and lowbirthweight,^{16,28-30,32-35} but the majority of these reports were retrospective, uncontrolled, orrelied on patient recall recruited later in the pregnancy. The largest prospective study was conducted by Weiss et al¹⁶. which concluded that first trimester bleeding was an independent risk factor for adverse obstetric outcome and it is also directly proportional to the amount of bleeding.

Type of Bleeding

In the present study, out of total 75 patients, 57 (76.0%) patients had complaints of pervaginal spotting and 18 (24.0%) patients had heavy vaginal bleeding. In the study by Kamble PD et al98, out of the 1007 females with First Trimester Vaginal Bleeding, 83.2% had spotting with abortion rate of 81.2%, whereas 16.8% had heavy bleeding with an abortion rate of 96.4%. In the study by Amirkhani Z et al27 96.6% patients had moderate to severe bleeding and 3.3% patients had spotting. Study by Rai P et al36 reported that out of total 100 cases withfirst trimester vaginal bleeding 70% presented with spotting while in the rest, heavy bleeding was observed. Another study by Patel NG et al37 reported that out of 100 cases with first trimester vaginal bleeding, 68% presented with spotting while 10% presented with heavy bleeding.

Incidence of spontaneous abortion, PPROM, preterm labour and low birth weight were more common in patients with 1st trimester bleed than 2nd trimester and in heavy bleeders than light bleeders within cases but none of the values reached conventional levels of statistical significance as a whole. Similarly, Weiss et al.16 and Chung et al.38 have reported that therisk of fetal loss was directly proportional to the amount of vaginal bleeding but they found an increased risk of preeclampsia after light bleeding, but strangely not after heavy bleeding. Most of the studies have failed to distinguish between light and heavy bleeding.

Subchorionic hematoma on USG

On ultrasonography, subchorionic hematoma was seen in 33 (44.0%) cases and 3 (4.0%) controls. This difference was found to be statistically significant (p<0.001). Pregnancy was aborted in 10 (30.3%) women with threatened abortion in which sub chorionic hematoma was seen on ultrasonography while pregnancy was aborted in 4 (9.5%) women without sub chorionic hematoma. Other maternal complications like APH (n=8; 24.2%), Preeclampsia (n=6; 18.2%), PPH (n=4; 12.1%) abruption placentae (n=3; 9.1%) and placenta previa (n=4; 12.1%) were more commonly seen in women with sub chronic hematoma compared to without sub chorionic hematoma. Kamble PD et al23 reported in their study that USG revealed sub chorionic hematoma in 74 patients of which 65 eventually aborted in spite of conservative management. 23% had incomplete abortion and emergency curettage was performed. 15.3% patients went up till term and delivered normally. Rate of abortion reportedin patients with sub chorionic hematoma was very high in study by Kamble PD et al23. Another study by Agarwal S et al31 also that very high percentage (43.55%) of patients had subchorionic hemorrhage on early USG in the cases while none in the control group had it, which was similar to our study. In their study 83.3% of spontaneous abortion was seen in patients with subchorionic hematoma compared to 16.66% in patients with no hematoma, even in cases. This result also confirmed the findings of Bennet et al39. The volume of hematoma influences the prognosis. In the study by Agarwal S et al31 high incidence (70%)of spontaneous abortion was seen with hematoma size > 4 cm2 and the rest 30% in patients with hematoma of size < 4 cm 2 but we did not see a relation between size of hematoma and rate of abortion. Patel NG et al37 also concluded from their study that in the presence of sub- chorionic hematoma, the prognosis of pregnancy is significantly affected as a risk of preterm labour, IUGR and especially miscarriages increases.

Spontaneous Abortion

An encouraging aspect of the current study was that patients with symptoms of threatened abortion and a living embryo that was documented are extremely likely to reach viability, while the incidence of spontaneous abortion is quoted to be 50% before sonographic evaluation for fetal viability.31 Out of 75 cases with threatened abortion, 14 (18.7%) patients aborted spontaneously whereas in 61 (81.3%) patients, pregnancy was continued; while in controls 3 (4.0%) patients aborted spontaneously and in 72 (96.0%) subjects pregnancy was continued. Similar to our study, Agarwal S et al31 also reported overall spontaneous abortion rate for the patients after a viable pregnancy as 21% in cases and 5.45% in control group. Another study by Yakıştıran B et al10 also reported higher rate of abortion in women with threatened abortion compared to controls. In contrast to our study Khanam M et al40 reported very high abortion rate in 100 cases of threatened abortion While in the study by Weiss et al16. the overall spontaneous pregnancy loss rate before 24 weeks of gestation was 0.5%. Thismay be explained by the later recruitment of the cases, when many of the early miscarriages would have already occurred. Another study which reported abortion rate similar to our study was done by Ahmed SR et al41 in which abortion rate

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in threatened abortion group was reported as 16.9% while in controls it was 2.2%. Over all 34% cases aborted and rest 66% pregnancies continued beyond 20 weeks of gestation in Rai P et al36study. Previous studies have also reported higher spontaneous abortion rates in study group compared to the control group. 15,42,43

Maternal complications

In 61 cases with threatened abortion where pregnancy continued beyond 20 weeks of gestation, the maternal complications were APH in 10 (16.4%) cases, placenta praevia in 5 (8.2%) cases, placental abruption in 5 (8.2%) cases, pregnancy induced hypertension in 8 (13.1%) cases and PPH was seen in 7 (11.5%) of cases. While in 72 controls, where pregnancy continued beyond 20 weeks of gestation, the maternal complications were APH in 5 (6.9%) cases, placenta previa in 1 (1.4%) cases, placental abruption in 2 (2.8%) cases, pregnancy induced hypertension in 4 (5.6%) cases and PPH was seen in 5 (5.6%) of cases. Although maternal complications were more common in threatened abortion group but difference was not found to be statistically significant. In the study by Kamble PD et al98 APH was observed in 1.8% and PIH in 5.5% cases which is lower than our study. Our finding was corroborated by Rai P et al36 who reported PIH in 15%, Abruptio placentae in 9% and placenta previa in 14% cases of threatened abortion. Patel S et al22 also reported that in patients where pregnancy continued beyond 20 weeks of gestation, the maternal complications were PIH in 6% cases, placenta previa in 3%, placental abruption in 7.5% and PPH in 6% of cases.

In the study by Agarwal S et al31, low lying placenta on USG before 20 weeks was seen in 16.13% patients in cases and 3.64% patients in control group. This difference between the groups was statistically significant (p = 0.02). But when the incidence was compared at 36 weeks there was no significant difference (p = 0.98). Our findings concur with previous studies by Weiss et al16. and Das et al30. This observation supports the concept of conversion of placental location with advancing gestational age for which different theories like placental migration, dynamic placentation and differential growth of lower uterine segment have been put forward. Whatever may be the mechanism involved, it operates in both groups. Thus it seems that low lying placenta plays a major role in causation of bleeding in early pregnancy. Weiss et al16 and Mulik et al33 observed a higher rate of placenta previa among patients with heavy vaginal bleeding during the first trimester. Because of impaired implantation and invasive trophoblasts, spontaneous abortion may occur in early pregnancy while preterm delivery, PPROM, placental ablation and preeclampsia mayhappen in later period.23 In the current study, the mean gestational age of patients at time of delivery in cases was 36.45 \pm 1.97 weeks and 38.13 \pm 2.08 weeks in control

group. This difference between the groups was statistically significant (p<0.01). Amirkhani Z et al27 found mean (\pm SD) gestational age at the end of pregnancy was 274 \pm 15 day in women with first trimester bleeding. In the study by Agarwal S et al31, the mean gestational age of patients in cases was 35.29 ± 3.48 weeks and 38.11 ± 4.77 weeks in control group. This difference between the groups was statistically significant (p = 0.0002) which may be partly due to higher incidence of preterm labour. Preterm delivery, is the leading cause of death of normal newborns44. Preterm prelabour rupture of membranes (PPROM) occurs in up to 40% of preterm deliveries.45

In our study, Women with threatened miscarriage had a significantly increased risk of preterm labour (less 37 weeks of gestation) compared with the control group (27.9% vs 12.5%, p=0.02). Risk of PPROM was also high in those women who have bleeding in the early pregnancy (9.8%) compared to controls (4.2%) but it was not statistically significant. Study by Agarwal S et al31 reported that women who have bleeding in the early pregnancy were at significantly increased risk of PPROM (20.41% in study group compared to 3.85% incontrol group) and preterm labour (28.5% in cases and 9.6% in the control group; p = 0.02). Our results are in agreement with the previous studies. 6,9,16,28,29,42,46 Similarly, Saraswat et al6 in a meta-analysis reported more likelihood to experience PPROM and preterm delivery instudy group. Another study by Strobino et al34 failed to show an association between pretermdelivery and threatened abortion. Kamble PD et al23 reported that in 15.3% cases preterm labour and in 6.75% cases PPROM was seen. Rai P et al36 also reported very high rate of PPROM (36%) in women with threatened abortion while preterm delivery was seen in 24% cases which is similar to our study.

Although the cause of PROM is unclear, Weiss et al16 gave a hypothesis that disruption of the chorionicamniotic plane by adjacent haemorrhage might make the membranes more susceptible to rupture by increased free radical production within the placental membranes. Alternatively, the prolonged presence of blood may act as a nidus for intrauterine infection. Another possible reason is that persistent or recurrent placental haemorrhage could also stimulate subclinical uterine contractions resulting in cervical changes and eventual ruptureof membranes.

The other point in etiology of PPROM is the chronic inflammatory reaction within the deciduas and placental membranes which causes rupture of the membranes, decidual thrombosis, ischaemia and necrosis results in vaginal bleeding along with inflammatoryresponse and thrombosis formation. Thrombin is a uterotonic agent and may cause preterm labour during late pregnancies and spontaneous abortion during early weeks of gestation.31

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Increased antenatal surveillance, possibly with cervical length measurements or the use of fetal fibronectin tests, might identify high risk cases within this group and will facilitate interventions, such as progesterone and antioxidant supplementation47 from a much earlier gestation and also decision making regarding management, for example, timely administration of antibiotics and corticosteroids or regarding mode, place and timing of delivery, which will inevitably improve neonatal outcome.42

Mode of Delivery

Among the 61 patients in whom pregnancy continued beyond 20 weeks, 60.7% of the patients had vaginal delivery and 39.3% had caesarean section while in among 72 controls,48 (66.7%) had vaginal delivery and 24 (33.1%) had caesarean section. In the study by Agarwal S et al31, incidence of LSCS done for various indications in cases was 32.65% compared to 28.85% in controls, which was not statistically significant (p=0.84). Kamble PD et al23 reported 41% caesarean section rate in cases with threatened abortion. Patel S et al22 reported 39% had caesarean section rate in cases with threatened abortion and the most common indication of LSCS was fetal distress (60%). Similar to our study, most of the previous reported same caesarean literature section rate.[6,30,48] In contrast, Sipila et al28 . reported a higher caesarean section rate in the cases with bleeding. The variability of results obtained in different studies seemed to be due to lack of consistencies observed between these studies, in the definition of the upper limits of abortion used, size of the study population, gestational age at presentation and to a lesser extent the statistical test used. It appeared that the definitive relationship between threatened miscarriages and adverse pregnancy outcome is not yet established. The positive value of this assumption raises the awareness of practitioners of the possible complications that may follow.

Saraswat L et al6 performed a systematic review and demonstrated that first trimester bleeding has no effect on route of delivery. But some other studies have shown that possibility of caesarean section in women with bleeding is more than others.23

Low Birth weight

Mean Birth weight is dependent on gestation, ethnicity, maternal weight and height. So all these confounding factors were standardised in both groups. Women with threatened miscarriage had significantly small babies with a mean birth weight (2476.75 \pm 386.35 vs 2803.60 \pm 366.43 gm, p<0.001). Similar findings were reported by Agarwal S et al31 in which mean Birth weight was significantly lower in the cases (2.47 \pm 0.69 kg) compared to controls (2.94 \pm 0.16 kg).

Babies weighing less than 2500 g were twice more common in cases (39.3% in cases v/s12.5% in controls). In contrast to our study, Kamble PD et al^{23}

reported only 11.5% low birth weight in their cases. The difference in mean birth weight seemed to be related to premature delivery, because a comparison of birth weights by gestation showed no difference between the groups, and the incidence of documented fetal growth restriction between the 2 groupswas also not significant. Dadkhah et al⁴⁸ and Haddow et al⁴⁹ also obtained similar results. Low birth weight rate was also high in the study by Rai P et al³⁶ (37.8%). Another study byPatelSet al²²also reported 36.3%low birth weight babies similar to our study.

It was seen in previous studies that due to numerous disorders of placenta in the pregnant women with first trimester bleeding, the length of pregnancy in these women is less and the possibility of premature delivery is more and as a result such pregnancies developed growth failure and newborn had low birth weight due to prematuredelivery.^{50,51}

Perinatal outcome

In 61cases with threatened abortion where pregnancy continued beyond 20weeks of gestation, manual removal of placenta was done in 3 (4.9%) cases, IUGR was seen in 6(9.8%), Intrauterine Death in 1 (1.6%), still birth in 2 (3.3%) and neonatal death was seen in 2(3.3%) cases. While in 72 controls, where pregnancy continued beyond 20 weeks of gestation IUGR was seen in 3 (4.2%), and still birth in 1 (1.4%) controls. Intra uterine death and neonatal death was not observed in any controls. Kamble PD et al²³ did not report any IUD in threatened abortion cases. In contrast to our study, Rai P et al³⁶ reported 14% had IUGR, and7% IUD in women with first trimester bleeding while Patel S et al²² also reported 13.6% IUGR and 9.5% perinatal mortality in women with threatened abortion.

As an opinion, lower APGAR scores after 1 and 5 minutes were expected in threatened abortion group because of increased rates of preterm delivery. Mean APGAR score at 1 minute and 5 minutes was lower in babies born to women with threatened abortion $(6.71\pm1.72 \& 7.64\pm1.91 \text{ respectively})$ compared with babies of women without threatened abortion $(7.21\pm0.75 \& 8.04\pm1.25 \text{ respectively})$ but it was not statistically significant. Out of 58 cases, NICU admission was required in 12 (20.7%) newborns while NICU admission was required in 7 (9.9%) controls (p=0.13). Kamble PD et al23 reported APGAR score <7 at 5 minutes in 4.3% cases. Rate of NICU admission was (30.6%) reported by Rai P et al36. PatelS et al22 also observed 30.3% NICU admission rate in these babies.

CONCLUSION

Concluding the result of present study, first trimester bleeding can be a predicting factor for late trimester pregnancy outcome; both maternal and foetal outcomes. It is therefore necessary to consider these pregnancies as a high risk group for which antenatal care should be performed carefully.

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