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The Effect of Threatened Abortion on Fetal Growth and Premature Rupture of Membrane

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ABSTRACT

Background: The diagnosis of threatened abortion is frequently made in clinical practice as a result of taking a history of vaginal spotting and the finding of a closed cervix at subsequent vaginal examination in first 20 weeks of gestation.

Objective: This study was conducted to evaluate the incidence and relation between threatened miscarriage and preterm premature rupture of membranes (PROM) and also its effect on fetal growth.

Patients and methods: The current study was conducted during a period of 8 months starting from 1st June 2019 till 31st August 2019. The patients were divided into two groups. First group: Included one hundred women presenting with threatened abortion at or below 20 weeks of gestation (case group). Second group: Included one hundred women who didn't have any symptoms of threatened abortion (control group). All patients were recruited from the Outpatient Clinics and Casualties of the Obstetrics and Gynecology Department, Al-Hussein and Bab Al-Sharia, Al-Azhar University Hospitals.

Results: Our study showed that there were significant differences regarding abortion, preterm labor and intrauterine growth restriction in the case group compared to the control group. There was a relative increase in the incidence of premature rupture of membranes, hypertensive disorders, placenta previa and the rate of cesarean section in the case group compared to the control group.

Conclusion: There was a relation between threatened abortion and adverse pregnancy outcomes.

Keywords: Threatened miscarriage, Fetal Growth and Premature Rupture of Membranes.

INTRODUCTION

Threatened abortion is defined as bleeding before 20 weeks of gestation, and occurs in around 20% of recognized pregnancies [(1)]. Approximately one-fourth of all pregnancies are complicated by bleeding before 20 weeks of gestation, and 12 to 57 percent of these pregnancies end in abortion [(2)].

The diagnosis of threatened miscarriage is frequently made in clinical practice through taking a history of vaginal spotting in first 20 weeks of gestation and the finding of a closed cervix at subsequent vaginal examination. A definitive diagnosis of threatened abortion should be made following ultra-sonographic examination, confirming the presence of fetal heart activity in an intrauterine pregnancy [(3)].

Bleeding during pregnancy can cause maternal anxiety and emerging evidence suggesting that it may be associated with poor fetal and maternal outcomes [(4)].

It is hypothesized that first-trimester bleeding may indicate an underlying placental dysfunction, which may manifest later in pregnancy causing adverse outcomes such as increased risk of pre-eclampsia, preterm delivery, preterm premature rupture of membranes (PPROM), placental abruption and intrauterine growth restriction (IUGR) [(5)].

While spontaneous rupture of membranes (ROM) is a normal component of labor and delivery, premature rupture of membranes (PROM) refers to rupture of the fetal membranes prior to the onset of labor irrespective of gestational age (can occur even at 42 weeks of gestation). Premature rupture of membranes may occur at term or immediately preceding labor, or it may be an unexpected complication during the preterm period, when it is referred to as preterm premature rupture of membranes [(6)].

Preterm Premature rupture of membranes (PROM) is a frequent obstetrical incident (3%) which can result in maternal and fetal complications such as infection and prematurity [(7)].

Pre-term, premature rupture of the membranes (PPROM) is the most common cause of pre-term labor (30-40%) [(8)].

AIM OF THE WORK

The aim of this work was to evaluate the effect of threatened abortion on fetal growth, premature rupture of membranes and on other adverse pregnancy outcomes.

PATIENTS AND METHODS

The current study was a prospective case-control study which was conducted during a period of 8 months, starting from January 1st, 2019 till August 31st, 2019.

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The current study included two hundred pregnant women. Patients were divided into two groups as follows:

Group 1: one hundred women presenting with symptoms of threatened abortion at or below 20 week of gestation, who had ultrasound examination afterwards and **group 2**: one hundred women who did not have any symptoms of threatened abortion. Patients were recruited in the study from the Outpatient Clinic and Causalities of the Obstetrics and Gynecology Department, Al-Hussein and Bab el-Sharia Hospitals, Al-Azhar University.

Ethical approval:

Research Ethics Committee and quality control approvals were obtained. The study purpose and procedures were explained in details and in plain terms to each of the subjects before being asked to give an informed written consent to participate in the study. Quality control of screening, handling of data and verification of adherence to protocols were done on a regular basis by the trial coordinator.

Inclusion criteria:

Pregnant women in first 20 weeks of gestation with single intrauterine pregnancy with sure last menstrual period that suffered from threatened abortion, diagnosed by vaginal spotting and minimal pain with closed cervix on examination and viable fetus by ultrasound.

Exclusion criteria:

Patients were excluded if they had chronic hypertension, diabetes mellitus, thrombophilia, smoking, history of recurrent miscarriage, congenital uterine anomalies, large leiomyomata distorting uterine cavity, cervical incompetence, local cervical pathology as cervical polyp, congenital fetal anomalies, maternal liver, renal and heart diseases, any patient that developed PPROM before 20 weeks (inevitable miscarriage) or developed fetal demise (missed abortion) , and any patient that was dropped-out during follow up program.

- **Patients were subjected to:**

1. Detailed history taking with special concern to obstetric history, last menstrual period for calculation of gestational age, past history (for any previous pregnancy complications or medical disorders) and family history.
2. Examination: general examination (focusing on the blood pressure to exclude pregnancy-induced hypertension [PIH], temperature, heart rate and respiratory rate). Body mass index, which was calculated according to the formula, BMI = weight Kg/ height M^2. Abdominal examination for fundal level and any sign of trauma and local vaginal examination to assess cervical dilatation.
3. Routine antenatal investigations included:
   - Complete blood count (CBC).
   - Fasting blood glucose and 2-hours oral glucose tolerance test.
   - Complete urine analysis.
4. Other laboratory investigations done to exclude some causes of fetal growth restriction:
   - Thyroid function (free T3, free T4 & TSH).
   - Kidney function tests (urea & creatinine).
   - Liver function tests (SGOT & SGPT).
5. Frequent ultrasound imaging throughout pregnancy till delivery includes:
   - Fetal life confirmation.
   - Fetal biometry for assessment of gestational age and presence of growth restriction.
   - Amniotic fluid index measurements.
6. Technique of ultrasound examination:

Trans abdominal ultrasound was performed to all patients while the probe was then tilted upward, keeping the indicator to the right, with appearance of the cervix and uterine fundus. The probe was continued to be tilted upward until the top of the uterus disappeared from view. After completing a transverse scan of the uterus, the probe was rotated clockwise so that the probe indicator was toward the patient's head, providing a longitudinal view. In this view, the bladder was seen anteriorly and inferiorly, with the vaginal stripe posterior. Using Logic V3 ultrasound machine with Doppler unit and convex linear transducer 3.5 MHz's. Sonographic parameters evaluated were; Size of gestational sac and CRL if < 12 weeks, fetal cardiac activity, sub chorionic hematoma, fetal biometry: BPD, FL, AC if >12 weeks, placental site, amniotic fluid index.

Statistical methods

Data were statistically described in terms of mean ± standard deviation and frequencies (number of cases) and percentages when appropriate. All statistical calculations were done using computer program SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft windows 2006.

RESULTS

In case group: patients who had spontaneous abortion (n=17) and patients that could not be followed up (n=25) were excluded and then we added 42 patients to the study with the same inclusion and exclusion criteria to complete the case group to 100 patients

In control group: patients who had spontaneous abortion (n = T) and patients that could not be followed up (n=15) were excluded from the study and then we added 16 patients with the same inclusion and exclusion

criteria to complete the control group to 100 pregnant women.

Occurrence of intrauterine growth restriction (IUGR) or premature rupture of membranes (PROM) were the primary outcomes.

The demographic data for the two groups are presented in table (2).

The mean maternal ages for the threatened miscarriage and the control groups were 28 ± 6.5 and 28.6 ± 6.1 years, (ranged from 18 to 40) years respectively. There was no significant difference concerning age distribution of the groups (p = 0.5). The mean parity for the study and the control groups were 2.4 and 2.5 deliveries respectively (p = 0.5). The mean gestational age at presentation for the threatened miscarriage group was 15.4 ± 2.4 weeks compared to 16.3 ± 2.2 in the control group.

Table (1): Comparison between both groups as regards the basic characteristics

Parameter (V**ariable)**	**Group 1 (Cases; n = 100)**	**Group 2 (Controls; n = 100)**	**P**
Mean Maternal age (years)	28 ± 6.5	28.6 ± 6.1	0.5
Mean Maternal BMI (Kg/M)	24 ± 3.3	25.3 ± 2.8	**0.003**
Mean Gravidity	3.6 ± 1.2	3.9 ± 1.4	0.1
Mean Parity	2.4 ± 1.1	2.5 ± 1.1	0.5
Gestational age (weeks)	15.4 ± 2.4	16.3 ± 2.2	**0.006**
Gestational age at time of presentation (weeks)	32.7 ± 2.4	33.8 ± 3.3	0.4

The overall adverse pregnancy outcomes were significantly higher in women with threatened abortion than the control group (Table 2).

Table (2): Comparison between both groups as regards the characteristics

Parameter (V**ariable)**	**Group 1 (Cases; n=100)**	**Group 2 (Controls; n=100)**	**P**
Maternal age (years)	28 ±6.5	28.6 ±6.1	0.5
Maternal BMI(Kg/M^2)	24 ±3.3	25.3 ±2.8	**0.003**
Gravidity	3.6 ± 1.2	3.9 ± 1.4	0.1
Parity	2.4 ± 1.1	2.5 ± 1.1	0.5
Gestational age (weeks)	15.4 ±2.4	16.3 ± 2.2	**0.006**
Gestational age(weeks)	32.7 ± 2.4	33.8 ±3.3	0.4
Fetal biometry (mm)			
BPD	32.5 ± 7.5	36.5 ± 7.3	**0.0002**
AC	100.7 ± 22.5	117.6 ± 25.4	**<0.0001**
FL	19.9 ± 6.6	25 ± 6.3	**<0.0001**
Mode of delivery			
Cesarean section	39	29	>0.01
Vaginal delivery	61	71	
Preterm birth	16(16%)	2 (2%)	<0.001
PROM	7 (7%)	4 (4%)	>0.3
Hypertensive disorders	6 (6%)	2 (2%)	>0.2
Placenta Previa	4 (4%)	0 (0%)	>0.1
IUGR'[2]'	11 (11%)	2 (2%)	<0.02
Cesarean section	39 (39%)	29 (29%)	0.1
Fetal birth weight (gm)	2335.1 ± 644.9	3118.9 ± 211.7	< 0.0001
Admission to NICU [(p)]	28 (28%)	7 (7 %)	<0.001

DISCUSSION

Bleeding in early pregnancy is a common obstetric complaint. These data showed that patients having threatened abortion had significantly increased risk of missed abortion, preterm labor and low birth weight. Other pregnancy complications such as placenta Previa, IUGR, PIH, PROM and cesarean section rates were relatively increased, but not at significant levels. Similar previous evidences were reported by **Saraswat *et al.* [9]**.

Our study showed no significant difference regarding the maternal age which is in agreement with **Davari [10]** who showed that the mean maternal age was (27.13 ± 4.76) in case group vs. (26.5 ± 4.52) in control group with p value 0.014.and this deference because there researches applied only on first 13 weeks of gestation and majority of previous researches were retrospectives.

Our study showed a significant difference regarding the maternal body mass index. Other studies did not refer to the maternal body mass index.

Our study showed no significant difference regarding the gravidity as the mean gravidity. **Davari-Tanha *et al.* [10]** reported a significant difference regarding the gravidity between case and control group with p value < 0.001, on contrary to that, **Dadkhah *et al.* [11],** found no relation between threatened abortion and gravidity.

Our study showed also no significant difference regarding the parity which is consistent with **Dadkhah *et al.* [11]** who found no relation between threatened abortion and parity.

Our study showed a significant difference regarding the gestational age (weeks) at time of presentation / examination but **Davari-Tanha *et al.* [10]** reported that the median onset of bleeding was at the 9th and 10th week of gestation in the high risk group and the low risk group respectively.

In the current study, there was an increase in the risk of spontaneous abortion in the case group vs. the control group. Our study showed that there was a significant difference regarding preterm labor as the incidence in the case group and this is similar to the results done by **Davari-Tanha *et al.* [10]** and is also similar to the study done by **Saraswat *et al.* [9].**

Our study showed that there was a relative increase in the rate of PPROM in the case group vs. in the control group (2%, 4%) respectively. **Saraswat *et al.* [9]** and **Davari-Tanha *et al.* [10]** reported a significant statistical difference regarding PPROM.

Our study showed a significant statistical difference in the incidence of IUGR in the case group compard to the control group. The infants of patients with threatened abortion had significant difference in birth weight when compared to the control group. **Davari-Tanha *et al.* [10]** reported an increased risk for IUGR in the case group.

Our study showed a relative increase in the incidence of hypertensive disorders as the incidence was 6% in the case group compared to 2% in the control group. This result is similar to the study done by **Davari-Tanha *et al.* [10]**.

Our data showed that there was a relative increase in the incidence of placenta Previa in the case group than in the control group), but **Davari-Tanha *et al.* [10]** showed that there was no increase in the incidence of placenta Previa.

Also, our study reported a relative increase in the incidence of cesarean section in case group than in control group. **Davari-Tanha *et al.* [10]** reported also a relative increase in the rate of cesarean section in case group than in control group.

Finally, our study showed a significant difference regarding the neonatal admission to NICU as the incidence was 28% in the case group vs. 7% in the control group with p value 0.001. This is similar to the study done by **Saraswat *et al.* [9]** who reported a significant difference regarding the NICU admission between both groups with p value 0.009.

The two studies mentioned above **Saraswat *et al.* [9]** and **Davari-Tanha *et al.* [10]** was different from our study in that our study was done on patients of threatened abortion at or below 20 weeks of gestation but the others did it on patients of threatened abortion in the first trimester only.

The literature reports on the association between bleeding in early pregnancy and pregnancy outcome is a conflicting one. Similarly, it was reported that the incidence of placental abruption, placenta Previa and premature rupture of the membranes were higher among patients with threatened miscarriage as compared to non-threatened group. Other evidence showed that such a relation is not yet established [12].

There is evidence that pregnancy complications, such as preterm labor and premature rupture of the membranes, may be due to impaired placentation and reactive oxygen species as a result of early pregnancy insult **[13].** This assumption is probably a risk rather than etiological factor, because it will not explain cases of premature rupture of the membranes and preterm labor seen in patients with non-threatened miscarriage. Therefore, it is still conceivable that other factors are

responsible for late pregnancy complications seen in threatened abortion group.

Lack of consistencies between these different studies was observed in 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 majority 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.

In conclusion the cause of majority is debatable, despite that several factors have been correlated with higher majority rates. In preterm labor, despite intensive researches, rates have not changed over the past 40 years. It is possible that more than one process is involved in the pathogenesis of these two conditions. One of the shortcomings on previous researches is that the majority were retrospectives. More prospective researches should be encouraged.

CONCLUSION

The current study reported that patients with threatened abortion are at increased risk for spontaneous fetal loss and adverse pregnancy outcomes as low birth weight, premature rupture of membranes (PROM), preterm labor, hypertensive disorders, placenta Previa and increased rate of C.S. So, the physicians should be aware of the adverse outcomes that may be associated with threatened abortion and should be alert for signs of these complications.

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