

## Causes of mid trimester pregnancy loss in a tertiary care hospital

Bushra Zardad <sup>1</sup>, Anisa Fawad <sup>2</sup>, Ayesha Ismail <sup>3</sup>, Shazia Mehreen <sup>4</sup>, Sadia Bibi <sup>5</sup>

<sup>1</sup> Registrar, Gynae A Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

<sup>2</sup> Professor, Gynae A Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

<sup>3</sup> Postgraduate trainee, Gynae A Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

<sup>4</sup> Medical Officer, Gynae A Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

<sup>5</sup> Registrar, Gynae A Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

### Author's Contribution

<sup>1</sup> Data collection, data analysis, data interpretation, manuscript drafting

<sup>2</sup> Manuscript writing, data interpretation, proof reading

<sup>3</sup> Literature search, data interpretation, write up, proof reading

<sup>4,5</sup> Data collection

### Article Info.

Conflict of interest: Nil

Funding Sources: Nil

### Correspondence

Anisa Fawad

draneesafawad@gmail.com

### A B S T R A C T

**Introduction:** Mid trimester of pregnancy is relatively a safe time of pregnancy with minimal and no complications. Mid trimester pregnancy loss constitutes 1 to 5 % of total miscarriages. The purpose of this study is to evaluate the causes of second trimester miscarriages so as to improve the outcome in future pregnancies.

**Materials & Methods:** This was a prospective cross-sectional study. Demographic features, relevant information and risk factors were recorded in a predesigned proforma. Detailed history was followed by thorough clinical examination and appropriate investigations were advised.

**Results:** Total number of miscarriages admitted in the unit over the period of two years were 336 and among them 30 patients presented with second trimester miscarriages (8.9%). The mean age of the patients was 31.4 years. In 19 patients (63.4%) there were identifiable causes for the miscarriage. 7 patients (23.33%) had fibroids in the uterus, 5 patients (16.67%) had bacterial vaginosis, 4 patients (13.33%) had cervical incompetence and in 3 patients (10%) there were congenital abnormalities in the uterus.

**Conclusion:** Patients with second trimester pregnancy loss are at significantly increased risk (10 times more likely) for recurrent second trimester loss. In 50 to 70% of patients no cause can be identified. After single loss there is 80% chance of successful pregnancy outcome in future. Even after two and three mid trimester losses still there is 60% chance of alive pregnancy next time, so thorough evaluation and management plan is needed to prevent this mishap in future pregnancies.

**Keywords:** Mid trimester miscarriages, fibroid uterus, bacterial vaginosis, cervical incompetence, congenital uterine abnormalities

**Cite this article as:** Zardar B, Fawad A, Ismail A, Mehreen S, Bibi S. Causes of mid trimester pregnancy loss in a tertiary care hospital. JSTMU. 2020; 3(2):64-69.

## Introduction

A second trimester miscarriage is defined as loss of pregnancy after 12 weeks' period of gestation and before 24 completed weeks. Mid trimester miscarriage is uncommon, comprising 1 to 5 % of total pregnancy loss. Second trimester miscarriage needs detailed evaluation especially where loss is recurrent to prevent such mishap in future pregnancies. In majority of patients (50 to 70 %)

the cause cannot be identified but it depends upon the resources available for thorough investigations.<sup>1</sup>

Sometimes there is more than one cause operating in one patient. The presence of multiple risk factors further increases the chances of mid trimester miscarriage and preterm labor. Common causes of second trimester miscarriage are incompetent cervix, abnormalities of uterus (fibroids, intrauterine adhesions), infections,

chromosomal and structural abnormalities in the fetus, chronic maternal medical disorders like uncontrolled hypertension, diabetes and disorders of thyroid gland, congenital uterine abnormalities, autoimmune diseases in mother, antiphospholipid syndrome and thrombophilias.<sup>2</sup>

Screening protocol includes detailed history, clinical examination and relevant investigations. In present pregnancy the period of gestation at which patient presented, along with her symptoms like history of uterine contractions, per vaginal bleeding, history of rupture of membranes and fever should be noted. Dating scan and anomaly scans should be reviewed along with any screening tests performed. Past medical history should involve enquiry about chronic maternal illnesses like hypertension, diabetes and disorders of thyroid gland. Family history of autoimmune diseases, thrombophilia, chromosomal abnormalities and congenital abnormalities should be noted. Past obstetrical history should be taken in detail especially regarding previous pregnancy losses, preterm deliveries, previous modes of deliveries and outcome of previous pregnancies. Examination should include both general physical examination and systemic examination. Abdominal examination should be followed by pelvic assessment. Vaginal swab should be taken for culture and sensitivity and ultrasound should confirm fetal viability.

Incompetent cervix classically presents with painless cervical dilation in absence of uterine contractions and alive fetus on scan. Studies have shown that fibroids in uterus, both submucosal and intramural, cause second trimester miscarriages. Congenital uterine abnormalities are uncommon but can be found in mothers with recurrent pregnancy losses. Screening for autoimmune diseases, antiphospholipid syndrome and thrombophilias should be done in mothers with recurrent second trimester pregnancy losses.<sup>3</sup>

This study was aimed to find out the cause of second trimester miscarriage for proper counselling and management of patients and to prevent recurrent losses in future. This study will aid to the existing knowledge about the subject and the results will be useful for practitioners to do evidence-based practice.

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## Methodology

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This was a prospective cross-sectional study conducted in Ayub Teaching Hospital, Abbottabad, OB/Gyn A unit, on patients who got hospitalized in the unit over the period of two years from January 2017 till December 2018. All the patients with first and second trimester miscarriages were included in the study. Written informed consent was taken and confidentiality was maintained. Study was conducted after getting approval from hospital ethical and research committee. Non probability consecutive sampling technique was used. Patients with twin gestation and polyhydramnios were excluded from the study.

Detailed history was taken followed by clinical examination. Previous history of miscarriages and preterm births was taken. History of congenital abnormalities and fibroids in the uterus as diagnosed on ultrasound was inquired. Clinical examination was done to exclude uterine myomas. Per vaginal assessment helped to exclude vaginal discharge and to determine cervical length and dilatation. Relevant investigations were sent which included abdominal ultrasound scan and high vaginal swab for culture and sensitivity. Data was collected by using a predesigned pro forma. Data was entered in and analyzed by using SPSS version 16. Mean was calculated for numerical variables like age. Frequencies and percentages were used for categorical variables. All results were presented in the form of tables.

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## Results

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Over the period of two years, the total number of miscarriages admitted were 336 including both first and mid trimester miscarriages. Among them there were 30 patients with second trimester miscarriage (8.9%) and 306 patients with first trimester miscarriages including threatened miscarriages. Among 30 patients with second trimester loss, in 11 patients (36.67%) no cause could be identified while in 19 patients (63.4%) there were identified causes. 07 patients (23.33%) had fibroids in uterus, 05 patients were diagnosed to be having bacterial vaginosis (16.67%), 04 patients (13.33%) had cervical incompetence and 3 cases (10%) had congenital uterine abnormalities. Majority of the patients were in age range of 25 to 35 years. Mean age was 31.4 years. 12 patients

were primigravidas (40%) and 18 patients were multigravidas (60%). Majority of patients had pregnancy loss between 18 to 20 weeks of gestation. The most common abnormality found was fibroids in the uterus, followed by bacterial vaginosis and cervical incompetence. Congenital uterine abnormalities were least common.

**Table 1: Age of Patients (n=30)**

Age	Frequency	Percentage
21- 25 years	5	16.67%
26-30 years	7	23.33%
31-35 years	8	26.67%
36-40 years	10	33.33%
<b>Total</b>	<b>30</b>	<b>100%</b>

**Table 2: Gravidity (n=30)**

Gravidity	Frequency	Percentage
Primigravida	12	40%
Multigravida	18	60%

**Table 3: Period of Gestation (n=30)**

Period of gestation	Frequency	Percentage
Less than 15 weeks	8	26.66%
18 to 20 weeks	15	50.00%
21 to 23 weeks	7	23.33%
<b>Total</b>	<b>30</b>	<b>100%</b>

**Table 4: Causes of Miscarriage (n=30)**

Cause of miscarriage	Frequency	Percentage
Unknown cause	11	36.67%
Fibroids	7	23.33%
Bacterial vaginosis	5	16.67%
Cervical Incompetence	4	13.33%
Congenital uterine abnormalities	3	10%
<b>Total</b>	<b>30</b>	<b>100%</b>

## Discussion

Second trimester pregnancy loss is uncommon but it is a distressing event in a patient's obstetrical history. It is the loss of pregnancy between 13 weeks to 23 weeks and 06 days' period of gestation. Patients with mid trimester loss are at significantly increased risk of recurrence (10 times more likely) of second trimester loss or preterm delivery in future pregnancy. In 50 to 70 % of patients no definite cause can be identified but it depends upon how thoroughly a patient has been evaluated and investigated. We received 30 patients with second trimester pregnancy loss over the period of two years and among them in 11 patients (36.6%) no definite cause could be identified.<sup>4,5</sup>

In 7 patients out of 19 (36.8%), there were fibroids in the uterus, both submucosal and intramural as diagnosed by ultrasound scan. A study was conducted in department of obstetrics and gynecology, CMH Lahore by Sarwat Navid and her team. They found 80 patients with fibroid uterus (equal to or more than 5 cm in size) in 10,842 OPD patients (0.74%). In this study 8/80 patients (10 %) had miscarriages. The conclusion of the study was pregnancy with fibroids is a high risk pregnancy with many complications including low lying placenta, placental abruption, breech presentation, cord prolapse, retained placenta, post-partum hemorrhage and need for emergency hysterectomy.<sup>6,7</sup>

A meta-analysis of different studies regarding fibroids and infertility by N Bajekal and T.C.Li has narrated that fibroids are fairly common in women of reproductive age group and are responsible for infertility and pregnancy losses. In women with fibroids, 50 % will conceive after myomectomy and there is a significant reduction in first and second trimester pregnancy loss. A submucosal or intramural fibroid distorting the uterine cavity, fibroids more than 5 cm in size and multiple fibroids are all indications for myomectomy in women planning the pregnancy.<sup>8,9</sup>

Infections have important role to play in mid trimester pregnancy loss and in preterm labor. 10 to 25 % of mid trimester miscarriages are caused by infections as discussed in different studies. Many infections are involved including bacteria, fungi, viruses, spirochetes and protozoa. The most important infection involved is bacterial vaginosis. It is imbalance in vaginal flora with

reduction in lactobacilli and abundance of anaerobes, enterococci, coliforms, staphylococci, fusobacterium, mycoplasma, ureaplasma, group B beta hemolytic streptococci and more importantly gardnerella vaginalis and mobiluncus. Bacterial vaginosis is present in 50% of pregnant women and is a risk factor for mid trimester miscarriage and preterm labor. In our study we found 5 patients out of 19 (26.3 %) with bacterial vaginosis as diagnosed by culture of high vaginal swab. Amsel criteria was used for diagnosis (thin, white, yellow, homogeneous discharge, clue cells on microscopy, pH of vaginal fluid >4.5). Treatment of bacterial vaginosis will reduce the incidence of mid trimester miscarriages and preterm deliveries. Studies have shown the beneficial effects of treatment for bacterial vaginosis if started before 20 weeks of pregnancy, so starting treatment early in second trimester is recommended.<sup>10-12</sup>

When cervical dilatation and effacement occurs without the presence of uterine contractions during second or third trimester before term, it is referred to as cervical insufficiency. True cervical weakness is an accepted cause of mid trimester pregnancy loss and preterm labor. In our study during the period of two years we received 4 patients out of 19 (21.2%) in which miscarriage occurred due to cervical incompetence as diagnosed by typical history of painless cervical dilatation and expulsion of alive pregnancy.

Ultrasound (transvaginal) assessment of cervical length is an effective prognostic indicator of mid trimester pregnancy loss and preterm labor especially in women with previous history. Cervical length less than 2.5 cm is best indicator in high risk patients. Such patients benefit more from cervical cerclage. A 02 years' study conducted in Ayub Hospital complex, Abbottabad showed high success rate of cervical cerclage applied in properly selected cases with previous history of mid trimester miscarriages and preterm deliveries, with sonographic evidence of cervical shortening, dilatation and cone formation.<sup>13</sup> A study conducted by Huma Naz and her team in Fatima hospital Baqai medical university Karachi studied beneficial effects of cervical cerclage in 33 patients. Patients with previous history of mid trimester pregnancy loss and preterm deliveries and those with cervical length less than 2.5cm on ultrasound were included in study. Pregnancy prolongation with delivery at

term occurred in 87.8% of patients.<sup>14</sup> Similar beneficial effects have been observed in several other studies.<sup>15,16</sup>

Elective cervical cerclage early in second trimester overcomes the risk of emergency procedure. A study conducted in Independent University Hospital Faisalabad over the period of two years included 50 patients with previous history of recurrent mid trimester miscarriages due to incompetent cervix. Effectiveness of cerclage was more than 90%. Elective procedure gives better fetomaternal outcome.<sup>17</sup> Elective cervical cerclage has definitely a beneficial role to play in patients with repeated mid trimester pregnancy losses, previous preterm deliveries with sonographic evidence of short cervix.<sup>18,19,20</sup> Although having beneficial effects for properly selected patients, the surgical procedure of cervical stitch application is not without risks. Saba Mubashir and her team studied the morbidities associated with this procedure in Agha Khan university hospital Karachi. It is 2 years' study which included 70 patients who underwent cervical stitch. Morbidities included rupture of membranes, miscarriages, preterm labor, chorioamnionitis and displacement of suture. Risk of maternal infection also rose by two fold. They reported that after cervical stitch application the risk of rupture of membranes was 10% and risk of miscarriage was 8.6%.<sup>21</sup>

In our study congenital abnormalities of the uterus were diagnosed in 3 patients of mid trimester miscarriages out of 19 (15.7%). There were 02 cases of bicornuate uterus and 1 case of unicornuate uterus as diagnosed by ultrasound scan. Structural abnormalities of the uterus are divided into the congenital abnormalities caused by abnormal fusion of mullerian ducts and acquired abnormalities which include fibroids in uterus, endometrial polyps and intrauterine adhesions. Uterine abnormalities cause miscarriages, preterm labor and intrauterine growth restriction. Congenital abnormalities of uterus include agenesis, hypoplasia, unicornuate uterus with or without rudimentary horn, uterine didelphys, complete or partial bicornuate uterus, complete or partial septate uterus and arcuate uterus.<sup>22-25</sup> Congenital abnormalities of uterus are diagnosed by 3 D ultrasound, hysterosalpingography and hysteroscopy.<sup>26,27</sup> The mean incidence in general population is 04% and in women with recurrent miscarriages the incidence is 06%. The true incidence in population is difficult to diagnose because

diagnostic tests are invasive and are done only in patients with infertility or recurrent pregnancy loss.<sup>28-30</sup> The role of hysteroscopy is both in the diagnosis and in treatment. Beneficial effects are seen in patients with repeated pregnancy losses after excision of intrauterine septum and adhesiolysis. Bicornuate uterus has highest incidence of first and second trimester pregnancy loss. Hysteroscopic resection is valuable in women with repeated losses.<sup>31,32</sup>

In first trimester of pregnancy 70% of miscarriages are due to chromosomal abnormalities while in second trimester 20 % are caused by this. Defects are usually trisomy, triploidy and monosomy. Ideally chromosomal make up of fetus and parents should be checked in recurrent first and second trimester miscarriages but this is not cost effective. In couples carrying balanced translocations, the risk of unbalanced translocation in the fetus is just 01% and live pregnancy rate is 70%, similar to general population. The presence of chromosomal abnormalities in the fetus or in parents' needs help of clinical geneticist and prenatal genetic diagnosis can be offered.<sup>33,34</sup>

Chronic maternal illnesses like uncontrolled hypertension, diabetes and disorders of thyroid gland all increase the chances of both first and second trimester miscarriages. Relevant history, clinical examination and appropriate investigations will help in diagnosis and management.<sup>35</sup> Antiphospholipid syndromes is present in 15% of patients with recurrent miscarriages. It is an auto immune hypercoagulable state caused by antibodies against cell membrane phospholipids that provoke blood clots both in arteries and veins. Antiphospholipid syndrome is associated with miscarriages, still births, preterm deliveries and severe pre-eclampsia. It is diagnosed by the presence of lupus anticoagulant and anticardiolipin antibodies in the serum.<sup>36,37</sup>

Thrombophilia screening should be done in all the patients having history of recurrent miscarriages in both first and second trimester. Low dose aspirin and low molecular weight heparin are treatment of choice if thrombophilia is associated with antiphospholipid syndrome.<sup>38</sup> Due to limitation of resources and poor socioeconomic status of our patients we were not able to perform some relevant investigations like screening for chromosomal abnormalities, thrombophilia and

antiphospholipid syndrome as investigations for these are not available inside hospital laboratories and pathology department.

## Conclusion

Second trimester miscarriage is a distressing event in any woman's obstetrical history. Detailed history, clinical examination and relevant investigations will help to find out the cause, so as to prevent future pregnancy loss.

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