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ADVANCED EXTRA-UTERINE PREGNANCY: CASE SERIES AND REVIEW OF 64 CASES REPORTED BETWEEN 1990 - 2016

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ABSTRACT

Introduction: Advanced abdominal pregnancy is a variety of ectopic gestation in which early diagnosis is missed and the pregnancy is allowed to advance beyond 20 weeks. It is associated with increased maternal mortality and morbidity.

Study: Meta-analysis and a report of 2 cases.

Results: The average age of women was 29 years. The most common presentation was persistent abdominal pain, abnormal lie, anemia and palpable fetal parts. Only 31% of the patients had risk factors for ectopic pregnancy. Sixty four percent of fetuses were born alive with a male to female ratio of 1:2.1. In majority of the cases the placenta was removed. In cases where the placenta was left in situ, the patients suffered more complications and had longer duration of hospital stay.

Conclusion: AAP is a rare but life-threatening conditions with possible catastrophic outcome. The basis of management lies in preventing maternal mortality and morbidity.

INTRODUCTION

Abdominal pregnancy is a variant of ectopic gestation with implantation within the peritoneal cavity exclusive of intra-tubal, ovarian and intra-ligamentous sites of implantation (1). Advanced Abdominal Pregnancy (AAP) is the growth and development of a fetus within the abdominal cavity beyond 20 weeks gestation (2). AAP are extremely rare with a reported incidence of 1 in 10, 000 deliveries but are significantly

higher in developing countries where there is poor antenatal care and monitoring (3) (4) (5). Advanced Abdominal Pregnancies are associated with increased maternal mortality (0.5 - 18%), maternal morbidity, fetal death (40 -95%) and fetal deformities which range from 0 – 100% (1) (6). Furthermore, diagnosis of abdominal pregnancy is difficult, especially where there is a low index of suspicion; this is compounded by inadequate diagnostic support especially in poor resource settings

with most AAP being diagnosed intra-operative (2) (6).

The aim of this study is to present two cases of advanced abdominal pregnancies and a meta-analysis of sixty-four cases.

METHODOLOGY

A search was conducted in Pubmed and Google scholar with Key words "Advanced Abdominal Pregnancy" and "Placenta". The title and abstracts were used to select articles to be included in the review. The full texts were then downloaded from Hinari and other open access journals.

Information extracted from the articles included: maternal age and parity, gestation at diagnosis and delivery, fetal outcome, management of placenta and complications arising from the management.

Analysis was done using SPSSv16, and descriptive statistics derived and presented in tables and graphs.

RESULTS

CASE: 1

A 38-year-old female, Para 3+0 Gravida 4, at 33 weeks 4 days gestation was referred to our facility with a one-month history of severe

progressive intermittent supra pubic pain radiating to the right flank. There was no history of vaginal bleeding, vaginal discharge, dysuria or fever. She reported being hospitalized at three months gestation due to severe anemia (Hemoglobin concentration of 5 g/dl) which was managed with hematinics. Her first delivery was a normal spontaneous vertex delivery 22 years ago, followed by a caesarean delivery due to poor progress in labor five years later and a normal vaginal delivery three years after. Her menarche was at 16 years; she reported having regular menstrual cycles with menses lasting four days, with moderate bleeding. She also reported having been on the second year of a five-year family planning implant when she realized that she was pregnant at three months gestation. Her vital signs were normal. Abdominal exam revealed a fundal height of 32 weeks in breech position, and a regular fetal heart rate at 144 beats per minute. An obstetric ultrasound revealed an empty bulky uterus and a single live extra-uterine pregnancy in breech with an estimated fetal age of 32 weeks and an estimated weight of 1833 grams (figure 1). The placenta was attached to structures in the pelvic cavity near the uterus.

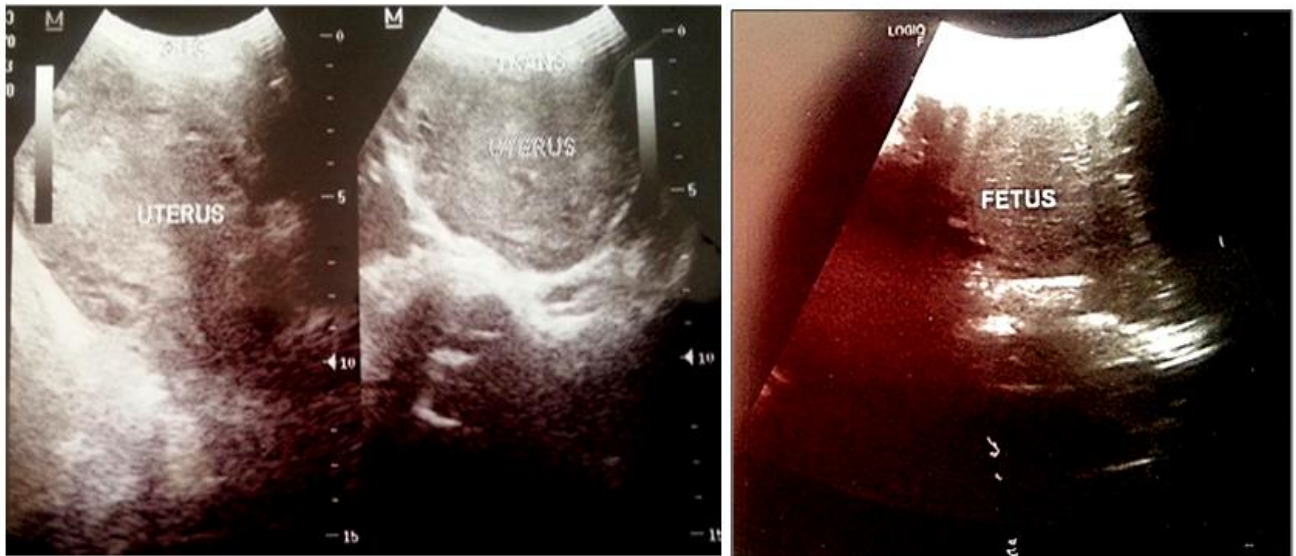


Figure 1: Pelvic ultrasound demonstrating empty bulky uterus with fetus within abdominal cavity

The patient was started on dexamethasone six mg twice daily for two days and intramuscular tramadol at 100 mg twice daily. Investigations on admission demonstrated a hemoglobin concentration of 10 g/dl. Urinalysis was negative for any infection. Delivery was scheduled at 34 weeks 2 days.

Intra operative findings revealed an abdominal pregnancy with a live infant within an amniotic sac with minimal liquor; the placenta was attached partially to the omentum, the right fallopian tube and part of the right ovary (figure 2).



Figure 2: Placenta attached to the right adnexa

A live male infant was delivered with an APGAR score of 9¹, 10⁵, 10¹⁰ and birth weight of 2.2 kg. The umbilical cord was clamped, and the placenta separated from its omental attachments with minimal bleeding. Right salpingo-oophorectomy was done to allow removal of the placenta. A tubal ligation on the left fallopian tube was also performed. On examination, the neonate was found to have facial asymmetry, a webbed neck and talipes valgus of the left foot. The mother did well post operatively and was discharged on the third day and is currently doing well.

CASE: 2

A 33-year-old Para 1+0, Gravida 2, with history of live birth and infant death at one year, presented at fifteen weeks gestation with supra pubic tenderness and severe symptomatic anemia. She had no history of contraception use. On first admission she was sick looking; with moderate pallor, blood pressure of 124/67 mmHg and pulse rate 117 bpm. Obstetric ultrasound at admission was suggestive of a bicornuate uterus with a normal intrauterine pregnancy in one horn and massive ascitis (figure 3).

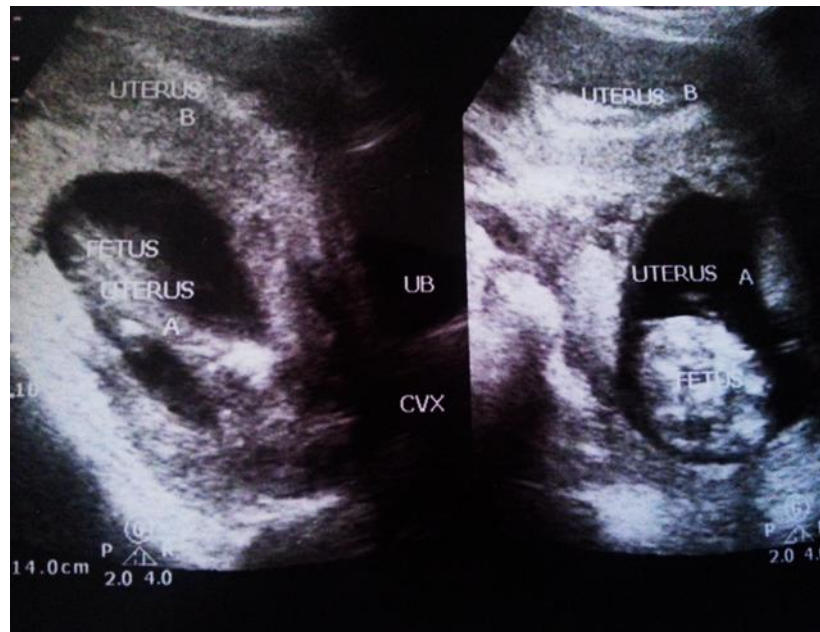


Figure 1: ultrasound image demonstrating a fetus in what was presumed to be one horn of a bicornuate uterus

A full haemogram revealed a microcytic hypochromic anemia of 5.5 g/dl. She was screened for urinary tract infection and intestinal nematodes, then transfused with 2 units pack cells and discharged after 10 days on hematinics. On the second visit at 30 weeks gestation, she complained of clear per vaginal discharge on and off for 3 weeks. On vaginal examination, there was an anterior closed cervix. A repeat ultrasound revealed a normal intrauterine pregnancy at 34 weeks with oligohydramnios. She was admitted and treated for anemia and vaginal candidiasis. She was also given dexamethasone 6 mg twice daily for two days then discharged. She was re-admitted two weeks (at 35 weeks 2 days) later with complaints of lower abdominal pains and a three-day history of per vaginal bleeding which had subsided to spotting. She was treated then discharged for follow up at the clinic. At 38 weeks gestation, she presented at the clinic with complaints of persistent spotting, lower abdominal pain and reduced fetal movements. On examination,

the fundal height was at 34 weeks, with a right sided pelvic mass and absent fetal heart rate. The cervix was 2 cm dilated in the anterior-lateral position. An immediate obstetric ultrasound confirmed intrauterine fetal death. The patient was admitted, and induction of labor was attempted using per oral misoprostol 25 micrograms every three hours. After two failed induction attempts, the patient was scheduled for a caesarean section. During the operation, a well-formed sac with thick membranes and a macerated fetus was found within the abdominal cavity. The placenta was partially adhered to the omentum and deeply to the uterine fundus. Part of the placenta attached to the omentum was removed in an attempt to arrest bleeding. There was an intra-operative blood loss of up to 2.5 Liters. Hemostasis was eventually achieved, and a drain was left in situ. Post-operatively, the patient was transfused with 2 units of whole blood and given a stat dose of methotrexate 30 mg three days later then discharged 15 days later. She presented a

month later with an abdominal swelling, and a tender palpable pelvic mass. A diagnosis of pelvic abscess was entertained and confirmed with a pelvic ultrasound. The patient was taken back to theatre where the abscess was drained. The patient was discharged 16 days post-operative and followed up in the clinic. She is currently doing well.

RESULTS OF LITERATURE REVIEW

A total of 64 cases of advanced abdominal pregnancies, inclusive of the cases reported here, were identified (Table 1).

Table 1

Parity of mothers with advanced abdominal pregnancy

Parity	Percentage (%)
1	33
2	27
3	16
4	6
>5	19

The average age of women presenting with advanced abdominal pregnancy was 29 years with a mode of 30 years. Seventy eight

percent of the women were aged between 20 to 34 years, with a peak between 30 to 34 years (figure 4).

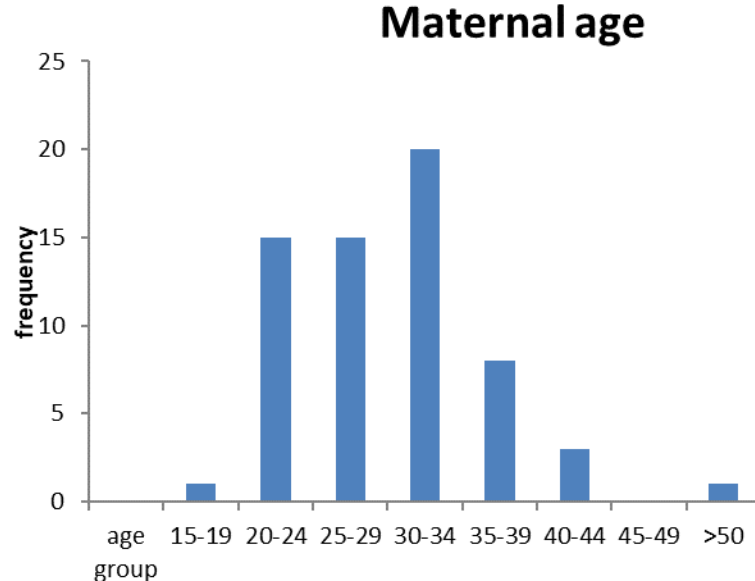


Figure 2: Maternal age distribution in Advanced Abdominal Pregnancy

The highest incidence of advanced abdominal pregnancy was in primigravidas at thirty four percent (21) (Table 1).

Table 2*Presentation in advanced abdominal pregnancy*

Presentation	Percentage (%)
Abdominal pain	63
Abnormal lie	31
Anemia	28
Fetal death	22
Palpable fetal parts	22
Per vaginal bleeding	19
Failed induction	19
Others	38

The most common presentation was severe abdominal pain throughout pregnancy (63%), followed by an abnormal lie (31%), anemia (28%), palpable fetal parts (22%), fetal death (22%), per vaginal bleeding (19%) and others (38%) inclusive of abdominal distention, ascitis, displaced cervix, hypotension, nausea, vomiting, peritoneal irritation, painful fetal movements, reduced fetal movements and respiratory distress (Table 2). A pre-operative diagnosis was made in 61% (39) of the cases.

Majority of the advanced abdominal pregnancies were secondary (75%) versus primary abdominal pregnancies at 7.8%. Only 31% (20 patients) of the mothers had risk factors for ectopic pregnancy.

On fetal outcome, 64% were born alive, with a total male to female ratio of 1:1.78, and a live male to female ratio of 1:2.1.

Expectant management was done in twelve cases, with two cases of fetal death and ten live births. Out of the twelve mothers managed expectantly, eleven were delivered between 26 weeks and 34 weeks, with only one case delivered at 38 weeks.

In 61% (38) of the cases, the placenta was removed, while in 32% of the cases, the placenta was left in situ with or without pre/post-operative embolization. In 7% of the cases, the placenta was partially removed.

Of those who had the placenta left in situ, 40% developed complications and 38% of them had a second operation. For those who had the placenta removed, 31% developed complication: the main complication (75%) being intra-operative hemorrhage (Table 3). Few studies reported blood loss; only six cases where the placenta was left in situ reported intra-operative hemorrhage (average 2,216 ml) while 14 cases where the placenta was removed reported an average blood loss of 1,235 ml. The average hospital stay for those who had placenta left in situ was 14.5 days, while those who had placentas removed was 9.36 days and 13.5 days for those with partial removal of the placenta.

DISCUSSION

Early recognition and diagnosis of abdominal pregnancy is key in averting associated maternal and fetal morbidity and mortality.

Risk factors include infertility, previous pelvic infections, congenital anomalies, endometriosis and previous history of ectopic gestation (1) (6); all which were absent in both our patients (7).

In the meta- analysis the most frequent complaints were abdominal pain, followed by an abnormal lie, persistent anemia, fetal

death, palpable fetal parts on abdominal examination, failed induction and per vaginal bleeding, (4). These features were notable in the both case reports. In the second case, the extra uterine pregnancy went unnoticed, therefore allowed to advance to term with subsequent loss of the fetus.

Ultrasonography is the most common and available imaging in most low resource centers (8). Ultrasound features suggestive of an extra uterine pregnancy include an empty uterus, with demonstration of a fetus within the abdominal cavity, oligohydramnios and hemoperitoneum (4) (9). However, ultrasound has a low sensitivity and specificity and is user dependent, evident in the misdiagnosis of the second case (1) (10). The gold standard for diagnosis is an MRI with maternal serum alpha fetal protein correlation. (9).

Laparotomy with immediate termination of pregnancy is highly recommended to prevent further placental invasion into maternal organs in addition to the associated high maternal morbidity and fetal mortality (9). However, expectant management allows more time for fetal maturation (6) (11). Only twelve cases were managed expectantly with two reported fetal deaths and ten live births. Most of the authors did not exceed 34 weeks except in one case where the mother was delivered at 38 weeks. Conservative management may be entertained in advanced pregnancies with a viable fetus and a stable mother, with maternal consent (12). Important factors to consider in expectant management are; maternal hemodynamic stability, fetal decompensation, hemorrhagic risk and placental site colonization. If the placenta colonizes the uterus or the uterine wall, the pregnancy may be allowed to advance because these sites provide a stable blood supply and the risk of spontaneous hemorrhage is low (10). In such cases weekly

MRI are recommended with planned elective delivery as close to term as possible (11). When the placenta colonizes sites such as the omentum, bowel, ovarian ligament, liver surface; active management is recommended. In the first case, diagnosis was made at 32 weeks but the placental site could not be accurately established, however she was admitted and active management initiated (6).

Most studies recommend an individualized approach to placenta management (10). The group which had complete removal of the placenta had fewer post-operative complications; the most common being intra operative hemorrhage. The group in which the placenta was left in situ had a longer hospital stay (average of 14.5 days) and a higher rate of complications (40%) with at least 19% of them being taken back to theatre for a second operation (13).

Complete removal of the placenta can be attempted if the placenta is attached to relatively avascular sites and where the blood supply to the placenta can be identified and ligated (8). Removal of the placenta is however, associated with a high intra operative hemorrhage risk (10) as seen in the analysis. Partial removal of the placenta is not recommended as it is associated with higher risks of intra operative hemorrhage (9) (11).

Conservative management of the placenta is recommended for cases where the placenta attaches to vascular organs, whereby an attempt at removing it would be catastrophic. Pre or post-operative embolization may also be done in suitable settings. If the placenta is left in situ, weekly evaluation for placenta involution with serial β hCG, weekly ultrasound or doppler studies, septic screen and physical examination are recommended (12). Leaving the placenta in situ has been shown to result in reduced maternal morbidity, shorter hospital stay, lower risk of

transfusion, and surgical menopause and is less costly (11), which is contrary to our findings. Leaving the placenta in situ is also associated with increased risk of pre-eclampsia/eclampsia, spontaneous separation of the placenta which might lead to massive secondary hemorrhage, development of ascitis or a pelvic abscess, need for a second surgery, failure of lactogenesis and a need for longer follow up (2).

The use of methotrexate has also come under criticism as it results in rapid degeneration of the placenta. This may result in secondary hemorrhage, and decomposing placental tissue acts as a nidus for infection which may result in pelvic/peritoneal infections (6) as was with our second case report. Some studies recommend leaving the placenta in situ without giving any post-operative medication to induce involution of the placenta with follow-up up to 2 years (10). Abdominal pregnancies are associated with a high fetal morbidity. Contrary to literature, 64% of fetuses in the meta-analysis were live births, with a live male to female ratio of 1:2.1. These findings are similar to a study by Masukume G were live female births

outnumbered live male births. This is consistent with the fact that males are generally more vulnerable to environmental insults during fetal development than females (14). Advanced abdominal pregnancies are associated with fetal deformities like facial asymmetry, severe webbing of the neck, elbow and knee, torticollis, hypoplastic limbs, joint deformities, talipes equinovarus and calcanovalgocavus. These are pressure deformities and are due to oligohydramnios (9). In our first case, we delivered a live male infant with facial asymmetry, a webbed neck and talipes valgus of the left foot.

CONCLUSION

An Advanced abdominal pregnancy is an extremely rare condition and is potentially life threatening. It is also difficult to diagnose as it presents with non-specific symptoms therefore clinicians need to have a high index of suspicion. A proper history and physical exam with advanced imaging modalities may provide a conclusive diagnosis. The basis of management lies in preventing maternal mortality and morbidity.

Table 3*Table summarizing management and outcomes of management of AAP*

Authors	Year of publication	Management of placenta	Complication arising from management
Tungsheninsirikul R et al.	1990	left in situ	none
Sapuri M, Klufio C	1997	left in situ	intra op hemorrhage
Motazedian Sh	2000	left in situ	intra op hemorrhage
Varma R et al.	2003	removal	none
Rahaman J et al.	2004	left in situ/ pre op embolization	none
Chitra KLS	2007	removal	none
Deeksha P et al.	2007	removal	none
Naim NM et al.	2008	removal	none
Isah AY et al.	2008	removal	none
Nunyalulendho DN, Einterz EM	2008	removal	none
Oneko O et al.	2009	removal	surgical site infection
Oneko O et al.	2009	left in situ	post-operative anemia, febrile episodes, abdominal pain
Oneko O et al.	2009	partial removal	re - laparotomy,
Dassah ET et al.	2009	removal	none
Oneko O et al.	2009	left in situ	none
Oneko O et al.	2009	removal	none
Meriem F et al.	2009	removal	none
Oneko O et al.	2009	left in situ	none
Oneko O et al.	2009	left in situ	none
Oneko O et al.	2009	removal	none
Amritha B et al.	2009	removal	none
Oneko O et al.	2009	left in situ	re operation due to severe abdominal pain - placenta removed
Gupta p et al.	2009	partial removal	intra op hemorrhage
Kshirsagar AY et al.	2010	removal	none
Yaliwal RG et al.	2010	removal	none
Hamid AN et al.	2010	removal	none
Yusuf N et al.	2010	removal	none
Leyva WR et al.	2011	left in situ	none
Brewster EM et al.	2011	removal	intra op hemorrhage
Eleje GU et al.	2011	removal	none
Leyva WR et al.	2011	removal	none
Dahab et al.	2011	removal	massive intra op hemorrhage
Farooq S	2011	removal	none
Leyva WR et al.	2011	removal	none
Kim MJ et al.	2012	partial removal	none

Smrtka MP et al.	2012	removal	neonate hospitalized for 5 months
Holder KP et al.	2012	left in situ/post-operative embolization	failed lactogenesis
Porwal S, Gupta R	2012	removal	none
Sharma R et al, 2012	2012	left in situ	none
Tungsagunwattana S, Poolsavatkitikool R	2012	removal	intra op hemorrhage
Mpogoro et al.	2013	left in situ	intra op hemorrhage, sepsis, prematurity with neonatal death, peritonitis, secondary hemorrhage, re- exploration
Mahbuba et al.	2013	removal	intra op hemorrhage, reverse talipes equinovarus
Meseci E et al.	2013	removal	intra op hemorrhage
Masukume G et al.	2013	removal	massive acitis with functional small bowel obstruction
Marcellin L et al.	2014	left in situ with post-operative embolization	none
Bohiltea R et al.	2014	removal	none
Matovelo, D et al.	2014	removal	aneamia, hemoperitoneum
Dabiri T et al.	2014	removal	intra op hemorrhage
Huang et al.	2014	left in situ	none
Joshi B, Aggarwal N	2014	removal	none
El Agwany et al.	2015	removal	intra op hemorrhage
Masri MA et al.	2015	left in situ	none
Bekabil TT; Geleta US	2015	removal	none
Brouard et al.	2015	left in situ	intra op hemorrhage
Gudu W, Bekele W	2015	removal	none
Harirah et al.	2016	left in situ	none
Bashir F et al.	2016	left in situ	intestinal obstruction, sepsis, required 2 nd surgery - [lacenta removed
Harirah et al.	2016	partial removal	intra op hemorrhage
Giwa Osagie et al.	2016	removal	none
Yeasmin S et al.	2016	removal	none
Sharma S et al.	2016	left in situ	none
Nassali MN et al.	2016	removal	intra op hemorrhage
Munguti CM et al	2016	removal	none
Munguti CM et al	2016	left in situ	intra op hemorrhage, pelvic abscess, second surgery

REFERENCE

1. Martin JN, Sessums JK, Martin RW, Pryor JA, Morrison JC. Abdominal Pregnancy: Current concepts of Management. *Obstetrics and Gynaecology*. 1988 April; 71(4).
2. Masukume G, Sengurayi E, Muchara A, Mucheni E, Ndebele W, Ngwenya S. Full Term abdominal extrauterine pregnancy complicated by post-operative ascites with successful outcome; a case report. *Journal of Medical Case Reports*. 2013; 7(10).
3. Rahman MS, Al-Suleiman SA, Rahman J, Al-Sibai MH. Advanced Abdominal Pregnancy - Observation in 10 cases. *Obstetrics and Gynaecology*. 1982 March; 59(3): p. 366 - 372.
4. Hamid AN, Begum R, Sultana Z, Akhler N. Advanced Abdominal Pregnancy: A Case Report. *JCMTCA*. 2010; 21(1): p. 74 - 76.
5. Dabiri T, Marroquin GA, Bendek B, Agamasu E, Mikhail M. Case Report: Advanced Extrauterine Pregnancy at 33 Weeks with a Healthy Newborn. *Biomed Research International*. 2014; 2014: p. 1 - 3.
6. Harirah HM, Smith JM, Dixon CL, Hankins GDV. Conservative Management and Planned Surgery for Periviable Advanced Extrauterine Abdominal Pregnancy with Favorable Outcome: Report of Two Cases. *American Journal of Perinatology Reports*. 2016; 6(3): p. e301 - e308
7. Yeasmin S, Begum T, Uggim M. Broad Ligament Pregnancy Through A Ceaserean Scar: An unusual one. *Chattagram Maa-O-Shishu Hospital Medical College Journal*. 2016 Jan; 15(1): p. 60 - 62.
8. Win T, Tang PH, Lim TYK. Clinics in diagnostic imaging (133). *Singapore Medical Journal*. 2011; 52(1): p. 53-59.
9. Mahbuba M, Fatema K, Saha RK. Advanced Abdominal Pregnancy with a Full - Term Live Fetus; A case Report. *Faridpur Medical College Journal*. 2013 January; 8(1): p. 40 -43.
10. Huang K, Song L, Wang L, Gao Z, Meng Y, Lu Y. Advanced abdominal pregnancy: an increasingly challenging clinical concern for obstetricians. *Int J Clin Exp Pathol*. 2014; 7(9): p. 5461 - 5472.
11. Brewster Sr EM, Braithewaite EA, Brewster Jr EM. Advanced Abdominal Pregnancy: A Case of Good Maternal and Perinatal Outcome. *West Indian Medical Journal*. 2011; 60(5): p. 587 - 589.
12. Marcellin L, Menard S, Lamau M, Mignon A, Aubelle MS, Grange G, et al. Conservative Management of an Advanced Abdominal Pregnancy at 22 Weeks. *American Journal of Perinatology Reports*. 2014; 4(1): p. 55 - 60.
13. Ojabo A, Hembraah-Helikan S, Audu O, Okoh E, Oka N. Outcome of Management of 5 Cases of Abdominal Pregnancies. *Open Access Library Journal*. 2015;(2): p. e1643.
14. Masukume G. Live Births resulting from advanced Abdominal extrauterine pregnancy, a review of cases reported from 2008 to 2013. *Webmed Central OBSTETRICS AND GYNECOLOGY*. 2014; 5(1).