Heterotopic pregnancies following natural conception; a review of four cases
Muhammad B. Aminu1, Lamaran M. Dattijo1, Aliyu U. Elnafaty2

SUMMARY
The occurrence of spontaneous pregnancy (viable or not) in one or more sites other than the endometrial cavity at the same time is an unusual phenomenon. We aimed to draw attention to the varied clinical manifestations and outcomes of heterotopic pregnancy (HP) amongst four consecutive patients who were managed in our facility over a two-year period. It is imperative for all clinicians to have a high index of suspicion for HP when seeing a woman of reproductive age with suspected ectopic.

Keywords: Spontaneous, heterotopic, pregnancy, diagnostic dilemma.

Department of:
1Obstetrics & Gynaecology, Abubakar Tafawa Balewa University Teaching Hospital, Bauchi Nigeria
2Obstetrics and Gynaecology, Federal Teaching Hospital, Gombe, Nigeria

Corresponding Author:
Aminu, B. M
Department of Obstetrics and Gynaecology
ATBU Teaching Hospital Bauchi
Mobile: +2347037147717
Email: aminubaffahmuhammad@gmail.com

Introduction
While ectopic pregnancy has remained relatively common in our region today, Heterotopic pregnancy (HP) in which there is the existence of both intrauterine and ectopic pregnancy, and which was hitherto thought to be rare is now emerging as a common clinical problem in our practice thereby posing both diagnostic and management challenges1,2,3,4.

Findings of HP are generally low worldwide with a reported incidence of 1 in less than 30,000 pregnancies5,2,4,6. This incidence tends to be narrowed to 1 in 100 among women that have had assisted reproduction2,7,8. Higher incidences of HPs had been demonstrated following pharmacological and surgical interventions like in-vitro fertilization but the incidence of HPs occurring spontaneously have not been widely reported7.

The diagnosis of HP is a challenge due to the uncertainty of B-hcg in the presence of both the intra and extra uterine pregnancies, but a transvaginal ultrasound scan is considered the best tool for the diagnosis9. Important intervention in HP is surgery which plays a key role in the management of the patient. However, care must be exercise during the intervention so that a viable intrauterine pregnancy will not be aborted10. This is the reason why laparoscopic surgery is preferred over laparotomy especially in a haemodynamically stable patient.
Four consecutive cases of women who were managed for spontaneous HP at Abubakar Tafawa Balewa University Teaching Hospital, (ATBUTH), Bauchi over a period of two years were presented. This is an attempt to highlight how common this condition is, its varied clinical presentations and management based on their various clinical manifestations.

**Case report 1**
A 32-year-old P6+1, 6A with eight weeks’ history of amenorrhoea, two days’ history of lower abdominal pain and vaginal bleeding, she had no history of fainting attack. She had previous left total salpingectomy one and half year before presentation for a ruptured ampullary ectopic pregnancy and had been on Depo injectable contraceptives for three years.

On examination, she had generalized abdominal tenderness, rebound tenderness and guarding. The uterus was not palpated per abdomen. There was a blood stained vulva but the cervix was closed. The uterus was about 8weeks size with right adnexal mass, and positive cervical excitation tenderness.

A trans-abdominal ultrasound scan showed a bulky uterus with a missed intrauterine gestational sac of 7weeks 6 days coexisting with a right adnexal gestational sac of 26mm with a visible fetal pole and cardiac activity. There was fluid collection in the Pouch of Douglas.

Packed cell volume (PCV) done was 24%. She had laparotomy with right total salpingectomy and manual vacuum aspiration later. Both samples were sent for histological analysis. Intra operative findings were that of haemoperitoneum of 700ml, bulky uterus of about ten week’s size, right ampullary ectopic pregnancy and about 30ml of Retained products of conception evacuated. She had two units of blood transfused. Histology report showed features consistent with ectopic pregnancy and that of decidua, chorionic villi and fibrin tissues for the intra uterine sample. She did well post-operative and was discharged after five days.

**Case report 2**
A 24-year-old P2+2, 2A with 6weeks history of amenorrhoea, one-day history of lower abdominal pain and vaginal bleeding associated with dizziness and fainting attack. She had no prior history of pelvic infections and the pregnancy was desired and spontaneously conceived. She had left total salpingectomy one year prior to presentation following ectopic pregnancy in the same facility.

On examination she was pale, with generalized abdominal tenderness, guarding and rebound tenderness. There was positive cervical motion tenderness.

Haematological investigations showed PCV of 26%. Urine pregnancy test was positive and an ultrasound scan showed free fluid in the peritoneal cavity. The uterus measures 4.9cm, with a right adnexal mass of about 4.0 x 5.0cm, a foetal echo with no cardiac activity. She had laparotomy, cornuostomy and uterine repair. Histology showed a fallopian tube that is dilated by large amount of haemorrhage; within this haemorrhagic background are chorionic villi and fibrin tissues.

She did well postoperatively but complained of having intermittent vaginal bleeding three weeks after the surgery, serial weekly serum beta HCG done were positive at (695mIU/ml, 1968mL/ml and 2341mL/ml). This was confirmed by a Transvaginal Ultrasound scan that showed a bulky retroverted uterus with a round sonolucent sac within the endometrial cavity 2.0 x 3.2cm in size; there was no foetal pole seen. The adnexa and pouch of Douglas were free.

She had medical management of missed abortion using Misoprostol 600 micrograms with complete expulsion. Histology report showed chorionic villi, deciduas, fibrin with areas of haemorrhage and necrosis in keeping with Products of conception. She did well subsequently and was discharged.

**Case report 3**
A 22-year-old primigravida presenting with a week history of excessive vomiting and lower abdominal pain, she had not seen her menses for six weeks five days. She had no history of vaginal bleeding, associated history of dizziness or collapse. She was admitted and managed for hyperemesis gravidarum with intravenous fluid and antiemetic. Her past medical history was...
uneventful. Index pregnancy was desired and spontaneously conceived.
She was a young lady in no obvious distress. There was mild supra pubic tenderness on abdominal examination. The uterus was not palpable per abdomen but there was positive cervical motion tenderness on pelvic examination.
Packed cell volume was 32% and serum Beta HCG was also positive (1580mIU/ml). A transabdominal ultrasound scan showed a viable intra-uterine gestational sac with a fetal pole of 5mm, approximately 6weeks 5days and a gestational sac in the right adnexum (GSD of 18mm) with a fetal pole but no cardiac activity. The pouch of Douglas was free.
She was managed conservatively. An ultrasound scan repeated at 13, 21 and 36 weeks of gestations showed normal viable fetus devoid of any anomaly. There was equally an exponential rise in the level of B HCG. She had an uneventful antenatal period and vaginal delivery of a live male neonate at term with a birth weight of 2.6 kilograms and good APGAR scores.

**Case report 4**
She was a 26-year-old P1+1, 1A with a 5-week history of amenorrhoea. There was associated abdominal pain and vaginal bleeding of 5 days’ duration. The pain was colicky with no known aggravating or relieving factor. There was no history of abdominal swelling and no history of surgical intervention. At the onset of the symptoms, she was seen and given injections at a primary health facility with some relief.
On examination, she was anxious. She had tenderness in the right iliac fossa. Pelvic examination revealed right adnexal mass with fullness in the pouch of Douglas.
Serum beta HCG was positive and PCV was 25%.
A transabdominal scan showed a bulky uterus measuring 58x60mm with AP diameter of 72mm. The endometrial cavity contained a distorted gestational sac measuring 18mm. The right adnexa had a gestational sac with a live foetus, crown rump length of 11mm equivalent to 7 weeks 2days gestation. There was significant fluid collection in the Morison’s and pouch of Douglas.
She had right total salpingectomy and Manual vacuum aspiration of the intra uterine pregnancy.
Findings from laparotomy were that of a bulky uterus with ruptured right ampullary ectopic pregnancy. The left tube and ovaries were normal; there was haemoperitoneum of 700ml. Histology report showed chorionic villi, deciduas, and fibrin from both samples. She had two units of blood transfused, subsequently did well and was discharged for follow up.

![Image](Fig 1 Showing a viable intra uterine and collapsed ectopic pregnancies)
Discussion

Heterotopic pregnancy occurs commonly with the extra uterine part within the fallopian tubes in about 70% of cases. It is rarer than ectopic pregnancy which itself was described as a great masquerade. The clinical diagnosis of HP is even more difficult despite the new knowledge and techniques for assisted reproduction. Physicians should, therefore, have a high index of suspicion in a woman presenting with rising level of human chorionic gonadotrophins (HCG) after uterine curettage or complete miscarriage or when the clinical estimation of fundal height is less than the gestational age in advanced pregnancy. The Beta -HCG levels may provide a clue to the diagnosis of spontaneously conceived HPs but not in similar pregnancies resulting from assisted reproductive technology due to the risk of Ovarian hyper stimulation syndrome (OHSS).

Similarly, the conflict between the exponential rise in Beta HCG early in pregnancy for extra uterine and that of a steady level in intra uterine pregnancy further deepen the challenge in the diagnosis of HP, this has led to the believe by some authorities that its use in the diagnosis of HP may not be objective. Just like ectopic pregnancy, vaginal bleeding is a common symptom and could occur in about 50% of cases of HP.

Identifiable risk factors for HP include previous tubal surgeries, pelvic inflammatory disease, use of intra uterine contraceptive devices (IUDs) and assisted reproduction, both surgical and pharmacological. In these series however, there was a low index of suspicion since the only risk identified was that of previous tubal operation and none of the patients was on ovulation induction drugs or In vitro fertilization; a technique whose contribution to this condition has been acknowledged.

The clinical presentation of HP varies, with either or both signs of normal and extra uterine pregnancy. In about half of all HPs however, there may not be any classic symptom and sometimes the symptoms could be non-specific. The cases highlighted above differ slightly with respect to the classical presentation of HP with vaginal bleeding occurring in three of the four patients presented. Similarly, the interval between the presentation of the four cases was equally short; an average of 2-3 month per case. This has never been reported to occur spontaneously and consecutively even among women that had assisted reproductive techniques (ART).

The majority of cases of heterotopic gestations can be diagnosed transvaginally between 5 and 34 weeks of gestation, and commonly with viable singleton foetuses. However, ovarian and cervical as well as higher order heterotopic gestations had been reported. The concept of ultrasound scan done early enough during evaluation of patients is helpful in the diagnosis of HP. Despite its sensitivity, ultrasound scan was diagnostic in only 26% of cases of HP compared to laparoscopy which was positive in over 70% of Cases. This is in contrast to our series where ultrasound scan was the major tool for diagnosis. An early ultrasound scan was indeed very helpful in the diagnosis of HP in our series. Additionally, the presence of foetal heart activity on ultrasound scan could further help in confirming the diagnosis especially if present in both sacs, though rare.

One of the biggest challenges in the management of HP is in the diagnosis though a rising HCG and fundal height had been enumerated. A careful ultrasound scan assessment of all patients should be done once there is history of amenorrhoea and a positive urine or serum pregnancy test, this is important because sometimes the gestational age may be difficult to visualized sonographically in a condition called pregnancy of unknown location. Just like the diagnosis, the treatment of HP is variable. In the majority of cases, the ectopic part is managed via laparoscopy or laparotomy, leaving the intrauterine pregnancy to continue especially if viable, resulting in the delivery of life neonates at term as seen in our third patient. Another treatment modality is the use of non-surgical options, where trophotoxic substances like hyper osmolar urea, methotrexate and potassium chloride can be injected mainly at the ectopic site to cause fetal reduction or demise by arresting trophoblastic activity, this can be done...
via laparoscopy or using ultrasound guided technique\textsuperscript{25,26,27,28}. The administration of methotrexate should be reserved for cases of HP with a non viable intra uterine gestation because of its lethal effects\textsuperscript{29}. The consensus in the treatment of HP, however, is the removal of the extra uterine pregnancy by the different approaches possible and the conservation and support for the intra uterine pregnancy where viable. However, if the ectopic site is not viable, a conservative approach can be done through serial ultrasound and HCG monitoring like it was done in case 3.

**Conclusions**

Spontaneous HP appears to be on the increase largely due to the high index of suspicion by the Physicians. Proper evaluation of the patients with amenorrhoea is the key to diagnosis and appropriate management. Clinicians should endeavor to rule out heterotopic Pregnancy once ectopic pregnancy is suspected.

**Ethical Issues**

The authors have obtained permission before using patient data and images.

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**References**


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