AUCTORES
Globalize your Research

Journal of Women Health Care and Issues

Anthony Kodzo-Grey Venyo *

Open Access

Research Article

Ectopic Pregnancy A Review and Update

Anthony Kodzo-Grey Venyo *, Olawumi Adaramodu

North Manchester General Hospital, Delaunays Road M8 5RB, Manchester, United Kingdom

***Corresponding Author:** Anthony Kodzo-Grey Venyo, North Manchester General Hospital, Delaunays Road M8 5RB, Manchester, United Kingdom

Received date: November 05, 2021; **Accepted date:** December 01, 2021; **Published date:** January 10, 2023

Citation: Anthony Kodzo-Grey Venyo, Olawumi Adaramodu (2023), Ectopic Pregnancy A Review and Update. J. *Women Health Care and Issues.* 6(2); DOI:10.31579/2642-9756/141

Abstract

Ectopic pregnancy is a terminology which is utilized for the scenario in which a fertilized eggs has implanted outside the uterus [5] which usually has tended to be within one of the fallopian tubes. The classical manifestations of ectopic pregnancy do include abdominal pain and bleeding per vaginam; nevertheless, it has been stated that less than 50% of women who are afflicted by ectopic pregnancy are stated to have both symptoms of abdominal pain and vaginal bleeding. The lady who has ectopic pregnancy could describe the abdominal pain as sharp pain dull pain, or crampy pain. The abdominal pain could also extend to affect the ipsilateral shoulder due to irritation of the diaphragm in the scenario of of bleeding from the ectopic pregnancy into the abdomen. Severe bleeding into the abdomen from ectopic pregnancy site into the abdomen or through the vagina could emanate in the patient developing a fast heart rate (tachycardia, fainting, or shock and on rare occasions the foetus may not have the chance to survive [6] When the patient who has ectopic pregnancy manifests with abdominal pain and bleeding from the vagina, the patient tends to be seen by a gynaecologist but when the patient presents with abdominal pain, loin pain or shoulder tip pain, the patient could in the first instance be seen by a General Practitioner, a general surgeon, a physician or a Urologist on rare occasions and hence even though ectopic pregnancy is a gynaecological practitioner, every clinician including General Duty Practitioners and Emergency clinicians need to have a high index of suspicion for ectopic pregnancy in order to establish a quick and accurate diagnosis to enable prompt and appropriate treatment of the patient. Some of the risk factors for the development of ectopic pregnancy do include: pelvic inflammatory disease, smoking of tobacco, previous tubal surgery, a history of infertility, utilization of assisted reproductive technology. In most hospitals globally, diagnosis of ectopic pregnancy tends to be established via utilization of blood tests for human chorionic gonadotrophin and the undertaking of ultrasound scan of abdomen and pelvis to demonstrate presence of the ectopic pregnancy. Nevertheless, in some small hospitals where facilities for ultrasound scan are not immediately available as well as in scenarios where serum beta human chorionic gonadotrophin are not immediately available on such rare occasions based upon a high index of suspicion for ectopic pregnancy the emergency general duty practitioner tends to subject the patient to surgical operation and during the procedure the ectopic pregnancy would be diagnosed and dealt with accordingly. Some of the differential diagnoses of ectopic pregnancy include: miscarriage, torsion of the ovary, appendicitis if the ectopic pregnancy is on the right side, rupture of corpus luteum cyst. Some of the treatment options that have been utilized for ectopic pregnancy include: surgery with various forms of surgical operation including salpingectomy, as well as achieving abortion via treatment with methotrexate. With regard to mortality associated with ectopic pregnancy the mortality has tended to 0.2%, but the mortality associated with ectopic pregnancy within the developing world has been 2%. Ectopic pregnancy is stated to account for 1.5% of pregnancies within the developed world.

Conclusion

- Ectopic pregnancy is a condition that tends to manifest with bleeding from the vagina plus abdominal pain but it could also manifest as abdominal pain alone and hence a patient with ectopic pregnancy may initially present to an emergency clinician, an obstetrician, / gynaecologists, a General Practitioner, a General Surgeon and on very rare occasions to a Urologist.
- A high index of suspicion is required to diagnose ectopic pregnancy based upon determination of serum Beta Human Chorionic Gonadotrophin levels as well as undertaking of ultrasound scan of abdomen and pelvis in order to provide appropriate and effective treatment based upon the clinical state of the patients as well as whether or not the patient has a desire to be pregnant again in the future.

- It is important to appreciate that a patient who has ectopic pregnancy could be seen for the first time by various clinicians including gynaecologists, emergency clinicians, general surgeons and even urologists. A lady who has pain in the right lower quadrant of the abdomen could be considered to have differential diagnoses, some of which include appendicitis, and ureteric colic and hence it is important to consider ectopic pregnancy as a possible diagnosis in cases of right sided lower abdominal and suprapubic pain
- Considering that occasionally a patient who has ectopic pregnancy may first be seen by non-gynaecologist it is important for all clinicians to have a high index of suspicion to exclude ectopic pregnancy when they see ladies in their reproductive ages who manifest with vaginal bleeding and abdominal pain or abdominal pain alone.

Key words: ectopic pregnancy; tubal pregnancy; uterus; fallopian tube; extra-uterine; rupture; bleeding; surgery; salpingectomy; methotrexate. morbidity; mortality

Introduction

Ectopic pregnancy is stated to be a terminology that is utilized for pregnanc y in which the developing blastocyst does implant outside the confines of th e endometrial cavity [1].[2]

It has been estimated that extra-uterine pregnancy does account for 1.3% to 2.4% of all pregnancies [1] [3] It has been iterated that 90% of ectopic preg nancies do occur within the fallopian tubes, and that the remaining ectopic p regnancies do tend to implant upon the cervix, the ovary, the myometrium, a nd other sites of the body. [1].[4] It has been pointed out that ectopic pregna ncy could manifest as abdominal or pelvic pain, amenorrhea with or withou t vaginal bleeding in the first trimester. It has also been pointed out that the minimum diagnostic requirement for an ectopic pregnancy is a transvaginal ultrasound scan as well as serological confirmation of pregnancy by the und ertaking of serum Beta Human Chorionic Gonadotrophin levels [1] [5] On r are occasions ectopic pregnancy may be diagnosed incidentally. A patient w ho has a ruptured ectopic pregnancy may manifest as having an acute abdo minal pain, hypotension, anaemia and would therefore require urgent resusc itation, transfusion and emergency surgical operation. A high index of suspi cion is required to diagnose ectopic pregnancy globally. Even though there are facilities for the undertaking of serum Beta-Human Chorionic Gonadotr ophin levels as well as trans-vaginal ultrasound scan and magnetic resonanc e imaging (MRI) scan in most health care establishments globally; neverthe less, facilities for the undertaking of trans-vaginal ultrasound scan and for a scertain serum Beta-Human Chorionic Gonadotrophin levels tend to be lack ing in some remote health care establishments in remote areas of some deve loping countries as well as transportation may not be easily available in suc h remote areas where medical practitioners may not be available but only m idwives and health care support workers and nursing staff only would tend t o be available. In remote health care centres that lack facilities for the confir mation of the diagnosis of ectopic pregnancy, an extremely high index of su spicion for the diagnosis of ectopic pregnancy does need to be on the minds of health care workers in order to refer patients who have suspected ectopic pregnancies so that the patients can be quickly referred on to secondary and tertiary health establishments quickly so as to avoid severe morbidity as wel l as death of patients who have ectopic pregnancy. A number of patients wh o have ectopic pregnancy would present with their symptoms to the General Practitioner (Family Practitioner) first who also need to have a high index o f suspicion for the diagnosis of ectopic pregnancy in order to refer the patie nts on quickly to the hospital for assessment and management. The ensuing article entitled ectopic pregnancy and review and update of the literature is d ivided into two parts: (A) Overview of Ectopic Pregnancy, and (B) Some su mmations related to some case reports, case series, as well as studies related to ectopic pregnancy.

Aims

To review and update the literature on ectopic pregnancy

Methods

Internet data bases were searched including: Google; Google Scholar; Yaho o; and PUBMED. The search words that were used included: Ectopic pregn ancy; Fallopian tubal pregnancy; Extra-uterine pregnancy; and ruptured ect opic pregnancy. Fifty-three (53) references were identified which were used to write the review and update of the literature on ectopic pregnancy which has been divided into two parts: (A) Overview of Ectopic Pregnancy, and (B) Some summations related to some case reports, case series, as well as stu dies related to ectopic pregnancy.

Results

[A] Overview

Definition / general [6]

- Implantation of the embryo outside of the uterine cavity including within the tubes (90%), abdomen and the cornua of the uterus [6]
- It has been stated that ectopic pregnancy does tend to occur in 1/150 pregnancies [6]
- It has also been stated that tubal pregnancies are the most common causes of haematosalpinx due to rupture which is a medical emergency and diagnosed with ultrasound, serum HCG and laparoscopy [6]
- It has additionally been stated that bleeding is sometimes due to placental separation without rupture [6]
- It has been pointed out that ectopic pregnancy is also referred to as an extrauterine implantation of a fertilized egg [7]

Other Terminologies – Other terminologies that have been utilized for ectopic pregnancy do include: [6]

- EP,
- Eccyesis,
- extrauterine pregnancy,
- EUP0,
- tubal pregnancy when the ectopic pregnancy site is within the fallopian.

Essential features of ectopic pregnancy [7]

The essential features of ectopic pregnancy have been summated as follows: [7]

- Ectopic pregnancy refers to extrauterine implantation of a fertilized egg

- Greater than 95% of ectopic pregnancies do tend to occur within the fallopian tube
- Diagnosis of ectopic pregnancy based upon visualization of an extrauterine gestational sac by transvaginal ultrasound (TVUS) or histologic confirmation

Clinical Manifestations [7]

Some of the clinical manifesting features of ectopic pregnancy had additionally been summated with explanations as follows:

- The commonest clinical manifestations do include first trimester vaginal bleeding or abdominal pain
- The presenting symptoms of ectopic pregnancy usually do tend to appear 6 weeks to 8 weeks pursuant to the patient's last menstrual period but the symptoms could occur even later, particularly if the pregnancy occurs outside of the fallopian tube
- No confirmed presence of intrauterine pregnancy

Epidemiology

- It has been documented that approximately 2% of all reported pregnancies within the United States of America (USA) are ectopic) [8]
- It has been iterated that 2.7% of pregnancy related mortalities had been attributed to ruptured ectopic [9]
- It has been documented that the diagnosis of ectopic pregnancy does tend to increase with age: 0.29% (15 - 19 years old), ~0.5% (20 - 24 years old), ~0.58% (25 - 29 years old), ~0.7% (30 - 34 years old) and ~0.89% (35 - 44 years old) [10]

Sites

- It has been iterated that the fallopian tube does account for 95.5% of extrauterine implantation sites of ectopic pregnancy: 2.4% occurs within interstitial sites, 11.1% occurs within fimbrial sites, 12.0% occurs within isthmic sites and 70% do occur within the ampullary site [11]
- It has additionally been iterated that 4.5% of ectopic pregnancies are of extra-tubal origin: 3.2% tend to be ovarian and 1.3% of the ectopic pregnancies tend to be abdominal [11]
- It has additionally been pointed out that ectopic pregnancy could implant at any place on the abdominal viscera or peritoneal surface: [12] Some of the documented places of implantation of ectopic pregnancy include the following:
    - Cervix [13]
    - Liver [14]
    - Spleen [15]
    - Previous caesarean scars [16]

Pathophysiology [7]

The pathophysiology of ectopic pregnancy has been summarized as follows: [7]

- Four (4) possible mechanisms of ectopic implantation had been documented including the ensuing: [17]
    - Anatomic obstruction which does prevent the passage of the zygote
    - Abnormal conceptus
    - Abnormalities of tubal motility.
    - Transperitoneal migration of the zygote.

Aetiology

It has been iterated that +50% of ectopic pregnancies are stated to be associated with pelvic inflammatory disease or peri-tubal adhesions (due to appendicitis, endometriosis, surgery and leiomyomas) [6]

Some of the aetiology factors for the development of ectopic pregnancy had also been documented to include the ensuing with associated explanations: [7]

- Pelvic inflammatory disease

  Disruption of tubal anatomy caused by infection is the most likely cause; inflammation of the tube is present in up to 90% of tubal pregnancies, which is 6x more common than in normal tubes
- Smoking of cigarette
- Previous fallopian tube pathology
- Infertility
- Insertion of Intrauterine device
- Previous fallopian tube surgery
- Previous ectopic pregnancy
- About half of ectopic pregnancy patients are stated not to have any identifiable risk factors

Miscellaneous Aspects

Miscellaneous aspects of ectopic pregnancy have documented in various articles including references [18] [9] [20] [21] [22] [23] [24] [25]

Laboratory tests undertaken in ectopic pregnancy to confirm the diagnosis [7]

- It has been pointed out that in cases of ectopic pregnancy the serum Beta HCG test results of the patients tend to be positive (high) [7]

Radiology imaging examination features of ectopic pregnancy [7]

It has been pointed out that radiology images in cases of ectopic pregnancy do demonstrate extrauterine gestational sac, with or without an embryo on transvaginal ultrasound [7]

General Diagnosis of ectopic pregnancy [7]

The mode of diagnosis of ectopic pregnancy has been summarised to include the ensuing: [7]

- The ascertaining of positive pregnancy test and visualization of an extrauterine gestational sac upon ultrasound scan, with or without an embryo on transvaginal ultrasound
- Visualization of presence of ectopic pregnancy during surgical operation with evidence of histopathology examination of confirmation of features ectopic pregnancy upon macroscopy and microscopy examination of the specimen

Macroscopy examination description typifying f ectopic pregnancy [7]

- Macroscopy examination finding of dilated tube with distended wall, with or without rupture

- Macroscopy examination of a specimen of ectopic pregnancy does demonstrate the lumen to contain blood clot, embryo, chorionic villi

Microscopy pathology examination description of ectopic pregnancy [7]

Microscopic (histologic) description

- It has been pointed out that even though not extensively studied, reports indicate a high prevalence of placenta accreta and percreta, to which tubal rupture is attributed [6]
- It has been stated that placentas from abdominal pregnancies have been described as highly vascular with markedly diminished / absent decidua [6]
- It has been pointed out that presence of extrauterine chorionic villi or extra-villous trophoblast is needed for diagnosis [7]
- It has also been iterated that in specimens of ectopic pregnancy, foetal tissue could be found present within the specimen. [7]
- It has been pointed out that endometrial stromal decidualization in isolation is not diagnostic of ectopic pregnancy
- **I**t has been iterated that in ectopic pregnancy, mesothelial reactive changes, often reactive mesothelial proliferation, might be present upon the surface of the fallopian tube or the closest peritoneum to the site of the ectopic pregnancy; and it has been pointed out to note that the exaggerated cytological changes and mesothelial proliferation should not be confused with atypical mesothelial proliferation [7]

Factors of prognostication in ectopic pregnancy. [7]

- It has been pointed out that there tends to be a significant risk of morbidity and mortality if ectopic pregnancy is not promptly recognized as well as treated [7]
- It has also been pointed out that patients who are found to have earlier ectopic pregnancies and relatively modest serum levels Beta HCG levels tend to be more likely to have successful treatment utilization of single dose methotrexate treatment. [19]
- It has furthermore been iterated that pursuant to methotrexate therapy, patients who do not exhibit at least a 15% decrease in the levels of their serum Beta HCG from day 4 to day7, tend to be more likely to experience treatment failure [20]

Treatment [7]

The treatment options of ectopic pregnancy have been summated to include the following: [7]

- Surgical management which does typically tend to entail the undertaking of salpingectomy or salpingotomy for hemodynamically unstable patients
- Methotrexate could be administrated as treatment for hemodynamically stable patients [19]
- Misoprostol could be utilized alone or in conjunction with another medicament (mifepristone or methotrexate) for the undertaking of medical abortion in cases of unruptured ectopic pregnancy as an alternative treatment to the undertaking of surgical treatment.

Differential diagnosis [7]

The differential diagnosis of ectopic pregnancy has been stated to be: [7]

- Spontaneous abortion:
  - It has been pointed out that in spontaneous abortion, there tends to be the identification of product of conceptions within the expelled uterine tissue or endometrial curettage tissue
  - It has also been explained that in spontaneous abortion, there tends to be lack of evidence of extrauterine gestational sac / embryo by either transvaginal ultrasound or histological confirmation

[B] Miscellaneous Narrations and Discussions from Some Case Reports, Case Series and Studies Related to Ectopic Pregnancy

Brancazio et al. [21] reported] a 29-year-old lady who was G4P3003, and who had manifested with bleeding from her vagina as well as discharged. She did not have any abdominal pain or any discomfort. She had a history of 3 caesarean section deliveries previously because of hypertension during her first pregnancy and 2 subsequent scheduled caesarean section deliveries pursuant to having normal pregnancies. Her most recent pregnancy was 3 years preceding her manifestation. She did not have any other significant past medical history other than having a body mass index (BMI) of 38, she did have regular menses, and she did not have any history of having had sexually transmitted infections. Three weeks preceding her manifestation, she had a trans-vaginal ultrasound scan within an outside her obstetrics appointment which had suggested presence of an intrauterine pregnancy at 7 weeks and 5 days with a gestational sac that was visualized within her lower uterine segment. During her manifestation, her vitals were found to be within normal ranges and stable. Her clinical examination was only documented to be notable for moderate clear-white discharge within her vaginal vault without blood and a closed cervix was found during her speculum evaluation. The results of her hemoglobin and haematocrit were documented to be within normal ranges, as was her white blood cell count. The results of her basic metabolic panel, wet prep, KOH, and STIs were noted to be negative. At her manifestation, the result of her quantitative Beta-HCG was 67,142 IU/L. Within an outside facility, she had undergone a transvaginal ultrasound scan which had demonstrated a single live intrauterine pregnancy low within the left uterine segment of her uterus with a 1.9 cm × 1.3 cm × 1.0 cm peri-gestational haemorrhage noted on the right of her gestational sac. She had transvaginal ultrasound scan which did not demonstrate free fluid within her pelvis. She had trans-vaginal ultrasound scan within her treating hospital which had illustrated a gestational sac that was dated at 10 weeks and 4 days which was located within the level of the internal cervical os. A foetal pole was noted with the presence of foetal cardiac motion. The gestational sac was documented to be located within an anterior position toward the anterior lower uterine segment at the level of her previous caesarean scar with little visible myometrium which was noted anterior to the gestational sac in her lower uterine segment. The gestational sac was reported to be found to be communicating with her endometrial cavity, while being located within the lower uterine segment of her uterus, and which was without involvement of the cervix. With regard for concern for her having a caesarean scar ectopic gestation, the possibility of implantation upon the previous caesarean scar in comparison with within the scar with lower risk of morbidity, and limitations of the ultrasound scan and given the maternal BMI of 38, an MRI scan was undertaken. She had MRI scan of her abdomen and pelvis without contrast which had demonstrated a gestational sac which was located within the anterior aspect of her lower uterine segment superior to the internal cervical os at the site of her caesarean scar. Disruption of the myometrium was reported to be suspected between the gestational sac and her urinary bladder, with only intact serosa of her uterus suspected, which was most consistent with implantation into her previous caesarean scar. Pursuant to discussion with the patient regarding her radiology imaging findings, potential complications of continuation of caesarean scar pregnancy, and reproductive goals, the patient iterated that she desired permanent sterilization. She did undergo an uncomplicated total laparoscopic hysterectomy with removal of the caesarean scar pregnancy, bilateral salpingectomy, and cystoscopy. She was discharged on her post-operative day 1 and she was scheduled to undergo close follow-up with obstetrics and gynaecology team. The authors made the following summating discussions: [21]

Figure 1: Sagittal transvaginal ultrasound showing an ectopic cesarean scar pregnancy (EGA 10 weeks, 4 days). The arrow indicates thinning of the anterior aspect of the myometrium. Reproduced from: [21] Brancazio S, Saramago I, Goodnight W, McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case Rep. 2019 Feb 2;14(3):354-359. doi: 10.1016/j.radcr.2018.12.001. PMID: 31007806; PMCID: PMC6457063. https://pubmed.ncbi.nlm.nih.gov/31007806/ under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).

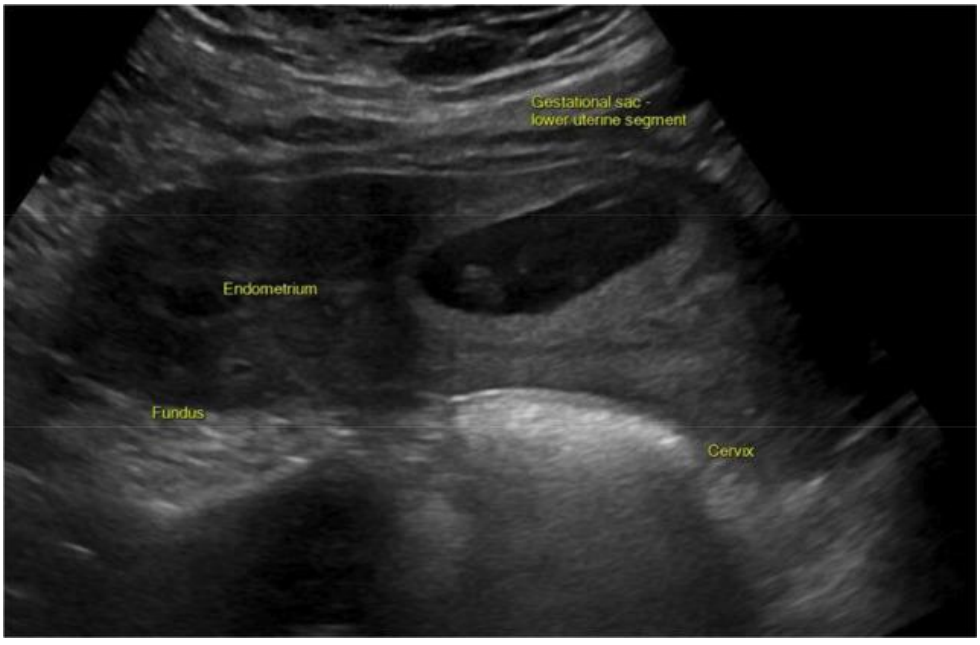

Figure 3: Sagittal trans-abdominal ultrasound demonstrating the characteristics of caesarean scar ectopic pregnancy: Low, anterior implantation of the gestational sac, absence of cervical involvement, extension toward the endometrium, and lack of normal endometrial cavity location. Reproduced from: [21] Brancazio S, Saramago I, Goodnight W, McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case Rep. 2019 Feb 2;14(3):354-359. doi: 10.1016/j.radcr.2018.12.001. PMID: 31007806; PMCID: PMC6457063. https://pubmed.ncbi.nlm.nih.gov/31007806/ under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).

- It has been stated that despite the fact that there are no specific diagnostic criteria for diagnosing caesarean scar ectopic pregnancies, ultrasound scan findings should indicate an enlarged lower uterine segment with thin myometrium at the implantation site. [24]
- Additionally, it has been iterated that the trophoblast should be located between the urinary bladder and anterior uterine wall, foetal parts cannot be located within the uterine cavity, and there should discontinuity of the anterior uterine wall on a sagittal view [27]
- Upon implantation upon the uterine scar, caesarean scar ectopic pregnancies could either extend into the cervical-isthmic space and into the uterine cavity (as occurred in their reported case study, or it could extend deeper into the myometrium toward to serosal surface of the uterus [26] Both forms of caesarean section ectopic pregnancy could emanate in in substantial haemorrhage, even though the latter also does tend to preclude a viable pregnancy, [26], [27].
- Hence it has been iterated that the suggested criteria for a caesarean scar ectopic pregnancy should include: (a) gestational sac that is embedded eccentrically within the lower uterine segment, (b) implantation in the location of a previous caesarean section delivery scar, (c) empty uterine cavity and cervical canal, (d) attenuated myometrium over the scar, and (e) extensive Doppler vascular flow in the area of the caesarean delivery scar. [28]
- Furthermore, Kaelin Atgen et al. [29] had distinguished implantation of the placenta into the previous caesarean section scar compared to attachment onto the previous caesarean section scar in the first trimester among continuing caesarean scar pregnancies. Implantation of the placenta into the scar and myometrial thickness that is less than 4 mm in the first trimester all had resulted in caesarean hysterectomy for morbidly adherent placenta, with lower birth weight and earlier gestational age at delivery among those who had implantation into the previous caesarean section scar.
- An MRI scan could provide additional confirmation of the ultrasound scan findings and characterize the myometrial interface if the pregnancy is difficult to distinguish from other complications of pregnancy including a cervical ectopic pregnancy or consideration for expectant management of pregnancy is considered (see figure 4, figure 5, and figure 6). [26]

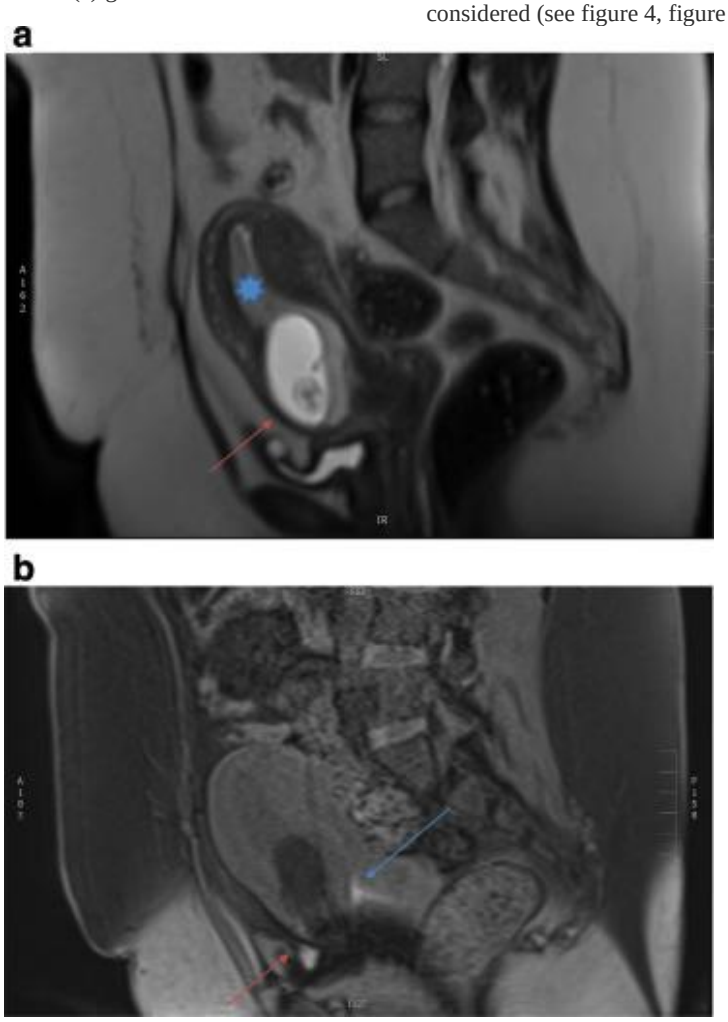

Figure 4: (a) Sagittal T2-weighted imaging demonstrating thinning of the anterior myometrium with low T2 signal (red arrow) and empty endometrial canal (*). (b) Sagittal T1 fat suppressed imaging demonstrating T1 hyperintense material in the pelvis (red arrow) and cervix (blue arrow) indicative of blood products. Reproduced from: [21] Brancazio S, Saramago I, Goodnight W, McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case Rep. 2019 Feb 2;14(3):354-359. doi: 10.1016/j.radcr.2018.12.001. PMID: 31007806; PMCID: PMC6457063. https://pubmed.ncbi.nlm.nih.gov/31007806/ under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).

Figure 5: Intraoperative image of uterus, round ligament and fallopian tube. The caesarean scar ectopic is noted deforming the left lower anterior wall of the uterus with increased vascularity (***). Reproduced from: [21] Brancazio S, Saramago I, Goodnight W, McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case Rep. 2019 Feb 2;14(3):354-359. doi: 10.1016/j.radcr.2018.12.001. PMID: 31007806; PMCID: PMC6457063. https://pubmed.ncbi.nlm.nih.gov/31007806/ under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).

Figure 6: Pathologic specimen following laparoscopic hysterectomy. Ectopic gestation is noted to the left lower uterine segment with disruption of the myometrium. Reproduced from: [21] Brancazio S, Saramago I, Goodnight W, McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case Rep. 2019 Feb 2;14(3):354-359. doi: 10.1016/j.radcr.2018.12.001. PMID: 31007806; PMCID: PMC6457063. https://pubmed.ncbi.nlm.nih.gov/31007806/ under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).

Even though ultrasound does remain the primary radiology imaging option for this diagnosis, MRI might be useful in the setting of equivocal cases and also MRI could aid in the detection of possible placental implantation or urinary bladder wall invasion. Sagittal T2-weighted MRI scan images are best for the visualization of the caesarean section scar, which does tend to appear as low signal. The radiology imaging features have been stated to include thinning of the myometrium in the region of the scar next to a gestational sac with a correspondingly empty endometrial canal and cervix. [30]

It has been stated that sagittal T2-weighted imaging could also be helpful in determining growth pattern of the gestational sac, for example, whether it is primarily within the scar or within the isthmus). This might have implications with regard to the management and risk of rupture [31]

Furthermore, T1 pre contrast imaging could be helpful with regard to the detection of blood products within the canal and pelvis.

Their reported case which they had presented in the article had highlighted the importance of early diagnosis and management of a caesarean scar ectopic pregnancy

Their reported patient's manifestation was similar to other reported cases that were found in the literature. She had manifested with painless first trimester vaginal bleeding. [27] [32].

Their reported patient's gestational age was also consistent with previous studies that had been reported indicating a manifestation between 5 weeks and 12 weeks of gestation. [26]

In view of the high clinical suspicion for a caesarean scar ectopic, the patient was able to undergo proper diagnosis and timely management.

Their radiology imaging findings had demonstrated the eccentric location of the gestational sac, implantation of the placenta into the prior caesarean scar and thin residual (3 mm) myometrium. As the patient in their reported case study had requested sterilization, surgical management was pursued with a total laparoscopy hysterectomy.

It has been iterated that with regard to patients who do desire fertility pursuant to their treatment of an ectopic pregnancy, clinicians could offer medical and more conservative surgical management uterine wedge dissection. [25]. [26]. It has been iterated that treatment of ectopic pregnancy with utilization of systemic methotrexate with or without intra-sac methotrexate could be undertaken in patients who have a gestational age of less than 8 weeks without foetal cardiac activity [26] [32] Nevertheless, it has also been documented that, medical treatment alone might leave the caesarean scar defect unrepaired and susceptible to complications during subsequent pregnancies. [26] [33]It has been recommended that physicians should counsel their patients who desire fertility pursuant to treatment of their ectopic pregnancies, as 30% of these patients have been documented to have difficulty conceiving pursuant to their ectopic pregnancy treatment. [34] It has furthermore, been recommended that clinicians should discuss the long-term risks of these pregnancies on subsequent pregnancies including the risk of recurrent ectopic pregnancy, rupture of the uterus, as well as placental attachment abnormalities. [24] Brancazio et al. [21] made the ensuing summations: Clinicians should continue to have a high clinical suspicion for a caesarean scar ectopic in a patient who has a history of caesarean deliveries who do manifest with first trimester bleeding. These patients should be diagnosed by means of the undertaking of trans-vaginal ultrasound scan with confirmation of the diagnosis by the undertaking of magnetic resonance imaging (MRI) scan if clinicians are not able to establish the diagnosis via the undertaking of ultrasound scan. In order to avoid the development of maternal haemorrhage, a patient who manifests with a caesarean scar ectopic pregnancy should undergo prompt treatment depending upon her clinical status and reproductive preferences.

Yoder et al. [35] made the ensuing iterations:

Ectopic pregnancy represents the leading cause of maternal morbidity as well as mortality during the first trimester of pregnancy and the incidence does tend to increase dramatically with assisted-reproductive technology (ART), and that ectopic pregnancy has tended to occur in approximately 1.5 % to2.1 % of patients who undergo in-vitro fertilization (IVF).

Abdominal ectopic pregnancy is an uncommon yet clinically significant form of ectopic pregnancy due to potentially high maternal morbidity.

- While risk factors for the development of ectopic pregnancy pursuant to IVF had been studied, very little was known about risk factors that are specific for abdominal ectopic pregnancy.
- They were reporting the case of a 30-year-old woman who had an abdominal ectopic pregnancy ensuing IVF and elective single embryo transfer, which was diagnosed and managed by laparoscopy.
- They had performed a systematic literature search in order to identify case reports of abdominal or heterotopic abdominal ectopic pregnancies after IVF and they had identified a total of 28 cases.

Yoder et al. [35] et al reported a 30-year-old G2P0010 who had manifested in their fertility centre seeking fertility treatment. She had a past medical history of polycystic ovarian syndrome (PCOS) and her partner had also had a diagnosis of male factor infertility. She did not have any previous surgical history, or any known allergies, and her medications had included prenatal vitamins. She denied having any history of sexually transmitted infections and she had a normal hysterosalpingogram and saline sonohysterogram. She had her first IVF cycle with an elective single embryo transfer that resulted in a negative pregnancy test. Her second IVF cycle utilized a GnRH antagonist stimulation protocol and she was triggered with Ovidrel on stimulation day 12. Twenty-two oocytes were reported to have been retrieved. On day five a single fresh blastocyst was transferred utilising a pass-through technique under ultrasound scan guidance. A stiff outer sheath was introduced via her cervix and past the internal os. A soft tipped catheter which contained the embryo was advanced via the outer sheath and the embryo was expelled into her uterine cavity about 1.5 cm from the fundus of her uterus with good visualization. Beta HCG was positive on her post-transfer day 9 and her serial Beta HCG values were monitored and which were noted to continuously rise appropriately. On day 28 after her embryo transfer, the patient had undergone a trans-vaginal ultrasound (TVUS) scan within the office which did not identify an intrauterine pregnancy (IUP) or any abnormal adnexal structures. She was asymptomatic with no vaginal bleeding or abdominal pain. She was sent for a more comprehensive ultrasound scan assessment at the associated Maternal Foetal Medicine unit and another Beta HCG result was obtained. She had a repeat ultrasound scan which similarly had failed to identify an intra-uterine pregnancy (IUP) or visualize an ectopic pregnancy. The result of her serum Beta HCG level was 12,400 pg/mL. Given her high serum Beta hCG level in the absence of an IUP, the patient was counselled and advised to take methotrexate therapy for a presumed ectopic pregnancy of unknown location. One day later which was on day 29, she received an intramuscular dose of 83 mg (50 mg/m^2 body surface area) of methotrexate with plans to follow her up with repeat serum Beta HCG estimations and trans-vaginal ultrasound scan (TVUS).

Four days following her methotrexate administration, she had a repeat serum Beta HCG level biochemistry test which continued to show a rise in her serum Beta HCG to 20,000 pg/mL and she had an ultrasound performed 1 day later which had demonstrated a right adnexal mass with a yolk sac, foetal pole, as well as foetal cardiac activity. The decision was taken to proceed with diagnostic laparoscopy for the treatment of ectopic pregnancy following failure of her methotrexate treatment. The patient continued to be asymptomatic with no evidence of vaginal bleeding or abdominal pain. She underwent diagnostic laparoscopy on day 34 post-embryo transfer. The operative findings were noted to be significant for minimal hemoperitoneum of less than 50 mL and her products of conception were observed to be implanted upon her peritoneum of the posterior cul-de-sac medial to her left uterosacral ligament (see figure 7). Her products of conception were removed utilizing graspers without difficulty and haemostasis was achieved with utilization of electrocautery and surgicel. All of her other pelvic organs including her uterus and bilateral ovaries and tubes had appeared macroscopically normal in appearance. **Figure 7**

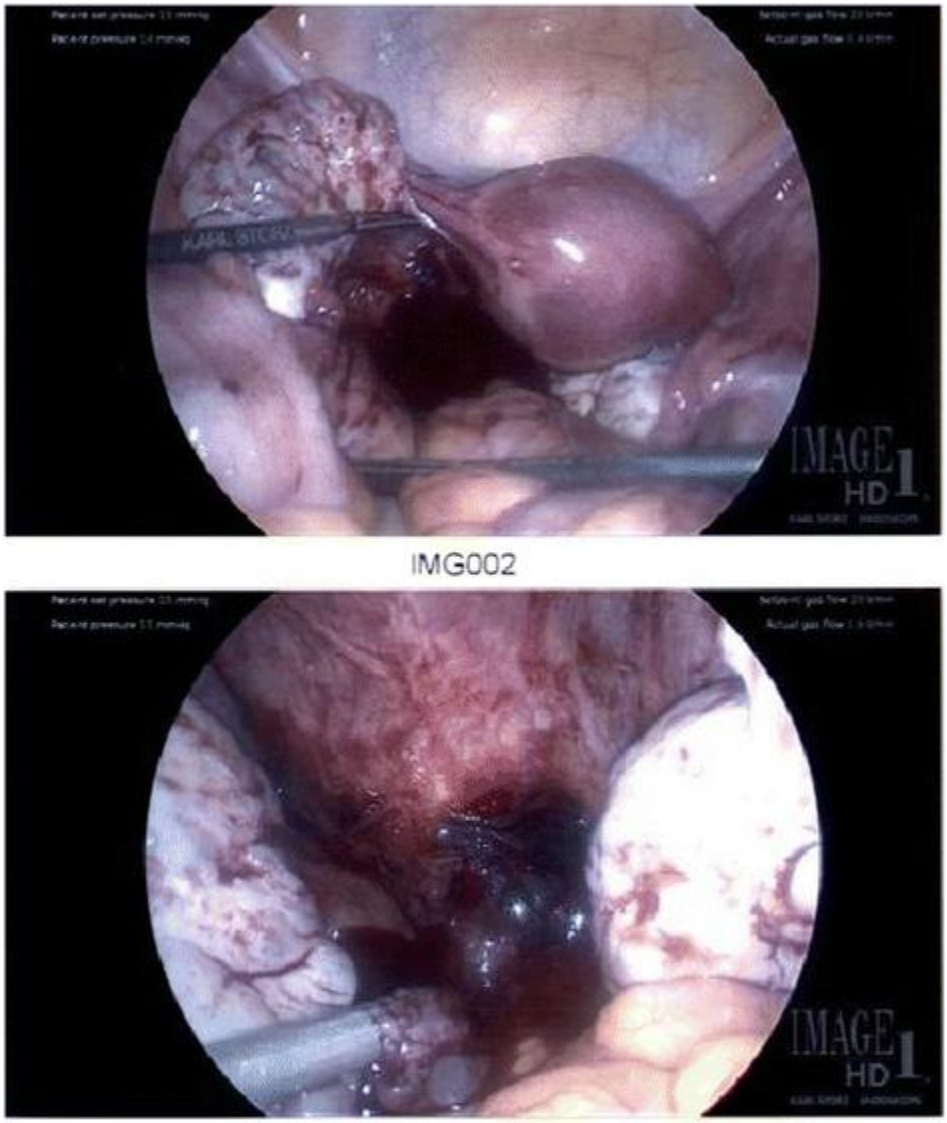

Figure 9: Diagnostic laparoscopy demonstrating hemoperitoneum (top image) and products of conception implanted in the posterior cul-de-sac (bottom image) Reproduced from: [35] Yoder N, Tal R, Martin JR. Abdominal ectopic pregnancy after in vitro fertilization and single embryo transfer: a case report and systematic review. Reprod Biol Endocrinol. 2016 Oct 19;14(1):69. doi: 10.1186/s12958-016-0201-x. PMID: 27760569; PMCID: PMC5070159. https://pubmed.ncbi.nlm.nih.gov/27760569/ under the Creative Commons Agreement Licence. (http://creativecommons.org/licences/by-nc-nd/4.0/)

Yoder et al. [35] summarized the results of their literature review as follows: as follows:

- The patients' ages had ranged between from 23 years and 38 years and the mean age of the patients was (Mean 33.2, S.D. = 3.2).
- Infertility causes of the ectopic pregnancy included tubal factor in 46 % of the cases, endometriosis in 14 % of the cases, male factor in 14 % of the cases, pelvic adhesive disease in 7 % of the cases, structural/DES exposure in 7 % of the cases, and unexplained infertility in 14 % of the cases.
- They had identified a history of ectopic pregnancy in 39 % of the reported cases. They had identified a history of tubal surgery in 50 % of the reported cases, and 32 % of the reported cases having had bilateral salpingectomy.
- Transfer of two embryos or more (79 %) and fresh embryo transfer (71 %) had been reported in the majority of cases.
- Heterotopic abdominal pregnancy had occurred in 46 % of the reported cases while 54 % of the reported cases were documented as abdominal ectopic pregnancies.

Yoder et al. [35] made the ensuing conclusions:

- Their systematic review had found several trends in reported cases of abdominal ectopic pregnancy following IVF with the inclusion of the following: tubal factor infertility, history of tubal ectopic and tubal surgery, higher number of embryos transferred, and fresh embryo transfers.
- These findings were consistent with the known risk factors for the development of ectopic pregnancy ensuing IVF.

- Additional research focusing upon more homogenous population might help in better characterizing this rare IVF complication and its risks.

Gari et al. [1] made the ensuing iterations:

- Ectopic pregnancy is a pregnancy which does occur outside the uterus, and which most commonly tends to occur within the fallopian tube.
- Ectopic pregnancy usually tends to be suspected if a pregnant woman does experience any of these symptoms during the first trimester of pregnancy: vaginal bleeding, lower abdominal pain, and amenorrhea. An elevated serum Beta Human Chorionic Gonadotrophin (Beta HCG) level above the discriminatory zone (2000 mIU/ml) with an empty uterus on a trans-vaginal ultrasound scan is essential for confirming the diagnosis of ectopic pregnancy.
- Such pregnancy could be managed medically with methotrexate or surgically through the undertaking of laparoscopy or laparotomy depending on the hemodynamic stability of the patient and the size of the ectopic mass.
- They were reporting the case of a 38-year-old woman, G3P2+0 who had manifested with a history of amenorrhea for three months. She was unsure of her last menstrual period and her main symptom was generalized abdominal pain. Upon examination, she was found to be clinically unstable and her abdomen was tender upon palpation and her abdomen was diffusely distended. Her serum Beta Human Chorionic Gonadotrophin (Beta HCG) level had measured 113000 IU/ml and a bedside pelvic ultrasound scan which was undertaken had shown an empty uterine cavity, as well as a live 13 weeks foetus that was measured by CRL. The foetus was found upon the ultrasound scan floating in the abdominal cavity and it was found to be encompassed by a moderate amount of free fluid, which was adjudged to be suggestive of ruptured tubal ectopic pregnancy. The patient's final diagnosis was live ruptured 13 weeks tubal ectopic pregnancy that was managed successfully by means of an emergency laparotomy with a salpingectomy.

Gari et al. [1] summarized details of their reported case as follows:

A 38-year-old lady, who was Gravida3 Para 2+0, had manifested to their emergency department with acute onset of lower abdominal pain that was associated with a history of amenorrhea for three months. She was not sure of the date of her last menstrual period and had not had any previous antenatal follow-up. She was noted to be medically free and her past obstetric history had included a normal uncomplicated vaginal delivery, which was ensued a caesarean section which had been undertaken four years preceding her current manifestation. She did not have any allergies and she had not been taking any medicaments or contraception. During her presentation, she had complained of having generalized lower abdominal pain which she reported was of a sudden onset, continuous, and which was not radiating to any other place, and which was not relieved by oral analgesia. She reported that her pain was associated with nausea and symptoms of anaemia including dizziness and shortness of breath, but she did not have any history of loss of consciousness, gastrointestinal or urinary tract symptoms. She did not have any history of fever or symptoms that were indicative of pelvic inflammatory disease. Upon her clinical examination, the patient was reported to look pale as well as distressed. Her blood pressure was noted to be 90/42 mmHg, and her pulse rate was documented to be 110 beats per minute. Her abdomen was found to be generally distended and she was found to be tender upon both superficial and deep palpation, with signs that were indicative of peritonitis. Her digital vaginal examination was reported to be positive for cervical motion tenderness and her serum Beta HCG Level had measured 113000 IU/ml. She had a bedside pelvic ultrasound scan, which demonstrated an empty uterine cavity and also as a live foetus that was floating within a moderate amount of free fluid in the pouch of Douglas. The result of her serum hemoglobin count was reported to have measured 3.2 g/L, and her total white cell count was 7.5 g/L. Her blood sample was taken immediately and sent for blood grouping and cross-matching of four blood units. With regard to diagnosis, the possibility of a ruptured ectopic pregnancy was explained to the patient, and she was consented to undergo an emergency laparotomy with possible salpingectomy. During her laparotomy procedure, a total of 4 litres of intra-abdominal blood was sucked out while blood transfusion was being undertaken. A live 13-week foetus was found and removed from her pelvic cavity, and the remains of the ectopic pregnancy including her gestational sac and placenta were found along a ruptured right fallopian tube. Her right fallopian tube was successfully resected, and the specimen was sent to histopathology examination. Both of her right and left ovaries were noted to look normal. Peritoneal lavage was undertaken completely, and a large pelvic drain was inserted. Histopathology examination of the fallopian tube specimen demonstrated chorionic villi within the lumen of the right fallopian tube, which was adjudged to be consistent with fallopian tube ectopic pregnancy. Intra-operatively, the patient did receive a total of five units of packed red blood cells as well as three units of fresh frozen plasma. She was transferred to the Surgical Intensive Care Unit (ICU) where she was observed for two days. During her stay within the ICU, she had remained hemodynamically stable. Her oxygen saturation was maintained with a 6L O2 face mask. Her chest was clear with bilateral equal air entry. Her abdomen was soft and lax, and her surgical wound was covered with a dressing. The pelvic drain was found to contain hemoserous fluid that measured about 450cc and her urine output was adequate. She had a repeated hemoglobin level post-transfusion and the result was 10 g/L, and her white blood cell count was 15 g/L. The results of her serum electrolytes were noted to be balanced and she was commenced on double antibiotic coverage together with and anti-stress medications. On her post-op day 3, she was transferred back to the general Gynaecology ward. She was discharged home in a stable condition five days pursuant to her surgical operation.

Gari et al. [1] made the ensuing summating discussions related to ectopic pregnancy:

- Ectopic pregnancy is a well-known complication of first-trimester pregnancy.
- It has been iterated that ectopic pregnancy is a potentially life-threatening condition and ectopic pregnancy is still considered as a major cause of maternal mortality, as ectopic pregnancy is responsible for 9% to 13% of all pregnancy-related deaths. [3]
- It has been pointed out that the vast majority of cases of ectopic pregnancies do implant within different locations within the fallopian tube, most commonly within the ampulla in 70% cases, followed by the isthmus in 12% of case, the fimbria in 11.1% of cases, and interstitium in 2.4% of cases. [36]
- It has been pointed out that many risk factors for the development of ectopic pregnancy have tended to be correlated with ectopic pregnancy such as previous ectopic pregnancy, tubal damage or adhesions from pelvic infection or prior abdominal-pelvic surgery, history of infertility, in vitro fertilization treatment, increased maternal age as well as smoking. Nevertheless, half of the women with ectopic pregnancies have no identifiable risk factors. [37]
- It is known that tubal pregnancy often has tended to become symptomatic within the first trimester of pregnancy in view of lack of submucosal layer within the fallopian tube wall which

does enable implantation of ovum within the muscular wall, that allows the rapidly proliferating trophoblasts to erode the muscularis layer. This usually tends to cause tubal rapture at 7.2 weeks ± 2.2, which then leads to haemorrhage and shock. Nevertheless, it has been pointed out that cases of advanced gestational age with different manifestations had been reported within the literature. Such events have been stated to be rare as it is unusual for the fallopian tube to dilate to the point of accommodating a second- or third-trimester foetus. [36]

- It has also been pointed out that ectopic pregnancy has remained a challenging diagnosis in an emergency department setting and in view of this, biochemical investigation including the undertaking of serum Beta Human Chorionic Gonadotrophin (Beta-HCG) levels and skilled ultrasound scan evaluation of the pelvis in a patient with a suspected ectopic pregnancy does play a vital role in acceleration and the management of patients who have ectopic pregnancy. [38]
- It has been pointed out that the decision related to the best treatment option of ectopic pregnancy does depend upon a number of factors including the patient's hemodynamic stability, serum Beta-HCG level, the size of the gestational sac, and patients' desire for future fertility. It has been documented that un-ruptured single ectopic pregnancies could be successfully treated with systemic methotrexate. [3]
- With regard to their reported case, an emergency laparotomy and a right salpingectomy, were undertaken in view of the ruptured ectopic mass, unstable hemodynamic status of the patient, as well as the accumulation of a large amount of intra-abdominal blood that was found upon the ultrasound image.

Gari et al. [1] made the ensuing conclusions:

- Even though it is unusual for an ectopic pregnancy to persist beyond the first trimester, it could occasionally occur.
- Hence, in all cases of surgical abdominal emergencies during pregnancy, it is important to exclude out ruptured ectopic pregnancy as ectopic pregnancy is life-threatening to the mother when the proper diagnosis and management are delayed.

Green et al. [39] reported that in 141 consecutive cases of tubal ectopic pregnancy that had been encountered within Hermann Hospital in Houston, Texas, United States of America, the histology examination appearance of 129 surgically removed fallopian tubes that contained ectopic pregnancies were reviewed as well as compared with an age- and race-matched control population. They reported that they found a higher incidence of chronic salpingitis in 88 versus 2%, and salpingitis isthmica nodosa in SIN 43 versus 5%. They additionally reported the ensuing results:

- The ectopic pregnancy patients did have a higher incidence of pelvic inflammatory disease, gonorrhoea, previous abortions, bi-tubal ligation, intrauterine device utilization, and previous abdominal surgery.
- In their study population, chronic salpingitis was the commonest associated finding.
- The increase in SIN was found to be associated with post-inflammatory changes that amounted to 89% of cases
- They also found that ectopic tubal pregnancies could grow either intratubally or extratubally by villous invasion into the wall and blood vessels; hence, surgical salvage of the fallopian tube by extracting the products of conception would not always be curative.

Saraçoglu et al. [40] studied excised tubal segments from 94 infertile women who had tubal obstruction, with a mean infertility duration of 5.3 years, and 40 women who had ectopic tubal pregnancy histopathologically in order to evaluate the association with salpingitis isthmica nodosa (SIN). Saraçoglu et al. [40] summarized the results as follows:

- The mean age of the 94 infertile women with tubal obstruction was 24.5 years.
- Hysterosalpingographies and laparoscopy had been undertaken on all of them.
- Only the women who had ectopic pregnancies in whom they had performed salpingectomy were included in their study.
- The incidence of SIN in women who had tubal obstruction was 7.4%, in women who had ectopic tubal pregnancy, it was 10%, and in the control group the incidence was found to be 0.2%.
- In 60% of the cases, SIN was found present in both of the fallopian tubes.

Saraçoglu et al. [40] concluded that based upon the results of their study, they had concluded that SIN is significantly associated with infertility and ectopic tubal pregnancy.

Majmudar et al. [40] reported that they had undertaken a prospective and retrospective study in order to analyse pathology lesions within fallopian tubes of 200 consecutive tubal pregnancies. Majmudar et al. [41] iterated that in a retrospective analysis of 100 cases of tubal pregnancy, seven cases were reported to contain salpingitis isthmica nodosa. Majmudar et al. [41] also reported the ensuing: After review, 27 cases were found to have this lesion. The prospective study had employed 100 consecutive tubal pregnancy specimens which were thoroughly sectioned for microscopy examination. Salpingitis isthmica nodosa was found in 57 of these 100 cases. In a control series of 100 fallopian tubes which had been obtained from autopsy and surgical specimens, five tubes demonstratedsalpingitis isthmica nodosa. Majmudar et al. [41] concluded that these observations had indicated a significant association between tubal pregnancy and salpingitis isthmica nodosa.

Lurie et al. [42] undertook a prospective study in order to test the hypothesis that microscopic chronic salpingitis is an aetiology factor in ectopic (tubal) pregnancy that is associated with an intrauterine device (IUD). Lurie et al. [42] summarized the patients and methods and results of their study as follows:

- Fifty consecutive patients at a university hospital who had been operated for tubal pregnancy fulfilled strict histological diagnostic criteria for tubal pregnancy.
- There were no statistically significant differences in prevalence of microscopy findings of chronic inflammation in patients who had never utilized an IUD, had a history of IUD use, or had an IUD in situ at the time of laparotomy.
- Salpingitis isthmica nodosa was found in four patients that amounted to 30.8% without past or present history of IUD utilization in comparison with two patients that amounted to 5.4% of patients who had a past or present history of IUD ($P < .05$).

Lurie et al. [42] made the ensuing conclusions:

- Utilization of an IUD did not appear to cause tubal pregnancy by the mechanism of tubal inflammation or presence of salpingitis isthmica nodosa.
- In view of this, other mechanisms by which an IUD might cause ectopic pregnancy should be considered.

Gayer et al. [43] studied a series of 89 Caucasian women, who had been operated upon for non-infectious tubal infertility in order to find out what contraceptive methods they had utilized before they had become infertile including oral contraception, intra-uterine contraceptive device and other methods. Gayer et al. [43] utilised a matched series of 178 fertile women as a control group. Gayer et al. [43] studied the numbers who had chlamydia as a function of the method of contraception in the group of infertile women. Gayer et al. [43] iterated that their work had shown that women who had tubal infertility due originally to infection had less often utilized oral contraception in comparison with the matched group of fertile women utilization. Gayer et al. [43] iterated that one could conclude that oral contraception does act as a prevention against this cause of infertility. Gayer et al. [43] also stated the following:

- The role played by intra-uterine contraceptive devices was difficult to establish.
- All the same, there was a significant relationship found between utilization of intra-uterine devices and tubal infertility of infectious origin, whether they looked at multiparae or women between 25 and 34 years of age.
- The results of their study also had shown that chlamydia was not associated with the use of combined preparation oral contraceptives, nor with the use of the intra-uterine device in women who have tubal factor infertility.
- The results of their study all the same had shown that it does appear to be important to advise utilization of oral contraception in preference to the intra-uterine device in women who still want to have a pregnancy, even if they are multiparae or multi-gravidae.

Gayer et al. [43] summarized salient points of their study as follows:

- The relationship between IUD and utilization of oral contraceptive (OC) and tubal infertility of infectious origin had been retrospectively studied in 89 French women who had undergone operations for tubal infertility between 1978 and 1987, 178 women who had spontaneously become pregnant regardless of the outcome constituted the control group, which was matched for age, social-professional status, and ethnic origin.
- Chlamydia trachomatis was found to be responsible for 73% of cases of tubal infertility. 22 of the 89 women did have a history of diagnosed salpingitis and 20 did have abdominal pain of unknown origin. 47 had not had any symptoms of salpingitis.
- The average age of the patients was 29.68 years for the tubal infertility group and 29.7 for the fertile women.
- The social-professional status of the 2 groups was found to be similar and higher than that of the general French population. 58% in the tubal infertility group and 36% in the fertile group were noted to be nulligestes. 60.1% of fertile women versus. 47.2% of infertile women had used OCs.
- More infertile women (22.5%) than fertile (14.6%) women had utilized IUDs; nevertheless, the difference was found not to be statistically significant. 45% of infertile women who had utilized IUDs did have a history of diagnosed salpingitis, versus 19% of pill and 18.5% of other contraceptive method users.
- The rate of chlamydia infection was found to be similar for OC, IUD, and other method users.
- The rate of utilization of IUDs was found to be similar for nulliparous fertile and infertile women, however, for multiparous women it was found to be significantly higher among infertile women. The finding that the infertile group had utilized OCs less often than controls did suggest that OCs have a protective effect against this type of infertility.
- The role of the IUD was harder to establish, however, a significant relationship was found between utilization of infectious tubal infertility and IUD among multiparas and among women aged 25-34 years.
- Their study had also demonstrated that chlamydia infections are not related to the contraceptive method that had been used.

Gayer et al. [43] concluded that in the light of their study it did appear important to advise utilization of OCs rather than IUDs for women who are likely to desire a future pregnancy, even for multiparous women.

Honore et al. [44] iterated that Salpingitis isthmica nodosa had been studied in relation to female infertility and tubal ectopic pregnancy. They iterated that the incidence of this lesion in a control Caucasian population was 0.6%, in comparison with incidences of 2.86% in an ectopic group and 50% in a small infertility group undergoing tuboplasty. Honore et al. [44] had suggested that salpingitis isthmica nodosa should be considered as an aetiological factor in these reproductive disorders. They also iterated that chronic tubal spasm had been suggested as the underlying process.

Bolaji et al. [45] stated the following:

- Salpingitis isthmica nodosa (SIN) is a nodular swelling of the isthmic segment of the fallopian tube.
- SIN is of unknown aetiology and it is usually an acquired pathological condition which has resulted from direct invasion of the muscularis layer by the endosalpinx in the isthmic portion of the fallopian tube between the lumen and the serosa.
- The clinical significance of SIN does rest upon its strong association with tubal ectopic pregnancy and subfertility.
- Assisted reproductive technology (ART) had improved upon the reproductive capability of SIN patients.
- Unlike ART, which does bypass pelvic pathologies, tubal surgical approaches improve fertility by correcting the pathology and can improve a patient's related symptoms of pelvic pain and abnormal menstruation, and provide a permanent cure.

Bolaji et al. [45] also stated that their article had provided an update on the epidemiology, aetiology, diagnosis and management of SIN and had concluded that despite the reported successes with tubal surgery, the mainstay of treatment does remain ART in (in the UK) centres recognised by the Human Fertilization and Embryology Authority (HFEA). The success of surgical infertility treatment does depend upon careful selection of cases utilizing appropriate investigative techniques, with the procedures carried out in centres with sufficient expertise.

Russell et al. [46] stated the following:

- The cause of ectopic pregnancy has tended to be associated with two major categories: the integrity of the oviduct and the quality of the fertilized ovum.

- Many conditions that alter the tubal transport system do include: inflammatory insults, intrauterine devices, surgical manipulation, tubal ligations, salpingitis isthmica nodusa, DES exposure, and induced abortions.
- Risk factors which could theoretically alter ovum quality or the hormonal environment do include ovulation induction, fertilization in vitro, delayed ovulation, and transperitoneal ovum migration.
- As clinicians continue to investigate the fallopian tube and the fertilized ovum as unique entities, the knowledge of clinicians would increase about the cause of ectopic gestations.

Russell et al. [46] presented the causes of ectopic pregnancy, which was divided into those arising from abnormal ovum transport and those due to abnormalities of the egg itself. They stated the following

- The fallopian tube is not a passive conduit, however, the active site of sperm capacitation, egg capture and fertilization are important.
- Conditions that result in damage to tubal lining such as salpingitis, even if it is subclinical as often occurs with Chlamydia, do increase the risk of tubal pregnancy.
- Other causes of damage to fallopian tubes do include vaginal douching, especially with commercial products, laparoscopic tubal ligation if it creates fistulas, even microsurgical reconstruction and conservative surgery for previous ectopic pregnancy.
- For unknown reasons, utilization of IUD, the thickening of the tube that is seen in salpingitis isthmic nodosa, and exposure to diethyl-stilbestrol also represent risk factors.
- Unresolved is the controversy that exists over whether previous induced abortions do predispose to the development of one ectopic pregnancy; possibly 2 or more abortions, or illegal abortions might adversely affect the statistics.
- Factors detrimental to ovum quality that tend to lead to ectopic pregnancy do include: induced ovulation, in vitro fertilization, delayed ovulation and migration of the ovum to the contralateral tube.

DeCherney et al. [47] made the ensuing iterations:

- The diagnosis of ectopic pregnancy had become precise and reliable.
- Hence, the management of ectopic pregnancy had progressed to the point where the physician has often been able to preserve fertility.
- In view of this, conservative surgery has tended to be indicated if the patient does desire future fertility and if the conditions are appropriate.
- The combination of utilization ultrasound scan, Beta-HCG pregnancy testing, and laparoscopy had led to a rising incidence of diagnosed ectopic pregnancy preceding rupture of the ectopic pregnancy. This had greatly facilitated utilization of the conservative approach to the management of tubal pregnancy.
- Even though ectopic pregnancy could be diagnosed early and managed conservatively, it is, and will remain a potentially life-threatening disease and should be approached as such.

DeCherney et al. [47] reviewed the manifestation, diagnosis, and treatment of ectopic pregnancy. They made the ensuing iterations:

- The current trend in the treatment of tubal ectopic pregnancy is aimed toward the preservation of reproductive function whenever possible.
- The incidence of ectopic pregnancy had not increased as much over the preceding several years as some reports had indicated; the discrepancy has been due to bias had been introduced by excluding numbers of abortions from the denominators.
- Pelvic inflammatory disease (PID) does represent the principal etiologic factor in the development of ectopic pregnancy, and Neisseria gonorrhoeae is the causative agent in majority of primary tubal infection.
- Patients who had undergone previous abdominal surgery, a history of PID, or who utilize IUDs do have more ectopic pregnancies.
- The clinical manifestation of ectopic pregnancy has tended to be variable, and women who have ectopic pregnancy could be asymptomatic.
- Any sexually active woman who manifests with abnormal bleeding, abdominal pain, or an adnexal mass should be examined immediately in order to exclude ectopic pregnancy.
- Culdocentesis could be used to determine whether intraperitoneal haemorrhage is present.
- The beta human chorionic gonadotropin (HCG) radioimmunoassay has remained unsurpassed as an endocrine test for the diagnosis of ectopic pregnancy however, it is time consuming.
- Diagnostic laparoscopy should not be postponed if a ruptured ectopic gestation is suspected.
- Ultrasound scan identification of an intrauterine gestational sac and a serum concentration of Beta HCG which hast exceeded 6500 IU/1 does rule out ectopic pregnancy.
- The finding of an ultrasound scan based normal uterus and a serum concentration of Beta HCG that does not exceed 6500 IU/1 is highly indicative of ectopic pregnancy.
- The undertaking of diagnostic laparoscopy in order to confirm the presence of tubal pregnancy had become routine since technical improvements had restored interest in the laparoscope in the early 1960s.
- Early diagnosis of ectopic pregnancy is crucial for the preservation of fertility.
- When a diagnosis of a tubal pregnancy is made, the physician needs to choose a radical or conservative approach of treatment based upon the patient's immediate medical condition as well as the patient’s desire for future fertility as well as the surgeon's experience.
- Salpingectomy does represent the procedure of choice if a fallopian tube is irreparably damaged or in the scenario if there is a hemoperitoneum that has been associated with shock or profuse bleeding.
- Rigorous cornual resection is not recommended in the surgical management of ectopic pregnancy because it does not exclude a

subsequent interstitial pregnancy and it might also weaken the myometrium.

- Colpotomy has rarely been indicated, and the removal of a normally functioning ipsilateral ovary is also not warranted.
- If a conservative approach to the treatment of ectopic pregnancy is feasible, salpingostomy and closure by secondary intention is the preferred treatment option over salpingotomy and primary closure, which could be complicated by bleeding and oedema. Fimbrial evacuation is the easiest procedure but Fimbrial evacuation has tended to be associated with the highest number of undesirable effects. Midsegment anastomosis, tubal-uterine implantation, and the Gepfert procedure have been noted to be either controversial or they have tended to be associated with poor prognoses.
- Of all conservative procedures for the treatment of ectopic pregnancy, only salpingostomy has tended to offer better results in term pregnancy rates in comparison with the radical operations.
- Salpingectomy is the most efficient treatment for the management of tubal gestation if the patient does not desire to have future fertility.

Tempfer et al. [48] stated that chronic ectopic pregnancy (CEP) represents a variant of ectopic pregnancy (EP) which is typified by low or absent serum human chorionic gonadotropin (hCG) levels, resistance to methotrexate (MTX), and an adnexal mass with fibrosis, necrosis, and blood clots related to repeated and gradual fallopian tube wall disintegration. They stated that CEP could complicate the course of patients with EP and CEP is difficult to diagnose. Tempfer et al. [48] reported the case of a 36-year-old woman who ha EP, low serum HCG levels, a small echogenic adnexal mass, and which was resistant to methotrexate (MTX). They reported a case in which Salpingectomy was undertaken and histology demonstrated CEP with fibrosis, necrosis, and a hematocele within degenerated chorionic villi. Tempfer et al. [48] summarized their review of the literature as follows:

- In a database search, Tempfer et al. [48] identified 19 case reports, 3 case-control studies, and 3 case series describing 399 patients with CEP.
- Serum HCG was found to be negative in 40 out of 124 cases that amounted to 32% with reported levels of serum HCG.
- The most common manifesting symptom was abdominal pain which was reported in 284 cases out of 399 cases that amounted to 71%, followed by irregular vaginal bleeding which was reported in 219 cases out of 399 cases that amounted to 55%, and fever in 20 cases out of 399 cases that amounted to 5%. 73 women out of 399 women that amounted 18% of the women were asymptomatic.
- An adnexal mass was found in 144 women out of 298 that amounted to 48% of cases with perioperative ultrasound examination and with a mean largest diameter of 6.8 cm.
- Data on treatment modalities and outcomes were available for to the authors on 297 women. Of these, 89% of the women had undergone surgery as first-line therapy. Laparoscopy was undertaken in most cases. Methotrexate (MTX) constituted the first-line treatment in a minority of cases. Complete resolution was achieved by first-line therapy in 287 cases out of 297 cases that amounted to 97% of cases. Adverse events had been reported in 218 patients who had CEP. Among those, adverse events ≥ grade 3 were observed in 186 out of 218 cases that amounted to 85% of cases. There was no case of reported treatment-related mortality.

Tempfer et al. [48] made the ensuing conclusions:

- CEP represents a variant of EP with low or absent trophoblast activity.
- A prolonged clinical course is typical and surgery is the mainstay of treatment for CEP.

MURRAY ET AL. [49] STATED THE FOLLOWING:

- ECTOPIC PREGNANCY IS A LIFE-AND FERTILITY THREATENING CONDITION WHICH IS COMMONLY SEEN IN CANADIAN EMERGENCY DEPARTMENTS.
- INCREASES IN THE AVAILABILITY AND UTILIZATION OF HORMONAL MARKERS, COUPLED WITH ADVANCES IN FORMAL AND EMERGENCY ULTRASOUND SCANNING HAVE CHANGED THE DIAGNOSTIC APPROACH TO THE PATIENT IN THE EMERGENCY DEPARTMENT WITH FIRST-TRIMESTER BLEEDING OR PAIN.
- ULTRASOUND SCAN SHOULD BE THE INITIAL INVESTIGATION FOR SYMPTOMATIC WOMEN IN THEIR FIRST TRIMESTER; WHEN THE RESULTS ARE INDETERMINATE, THE SERUM B HUMAN CHORIONIC GONADOTROPIN (B-HCG) CONCENTRATION NEED TO BE MEASURED.
- SERIAL MEASUREMENT OF B-HCG AND PROGESTERONE CONCENTRATIONS MIGHT BE USEFUL WHEN THE DIAGNOSIS DOES REMAIN UNCLEAR.
- ADVANCES IN SURGICAL AND MEDICAL TREATMENT FOR ECTOPIC PREGNANCY HAD ALLOWED THE PROLIFERATION OF MINIMALLY INVASIVE OR NON-INVASIVE THERAPY.
- GUIDELINES FOR LAPAROSCOPY AND FOR METHOTREXATE THERAPY DO EXIST FOR THE MANAGEMENT OF ECTOPIC PREGNANCY.

Sivalingam et al. [50] made the ensuing summating iterations related to ectopic pregnancy:

- It has been pointed out that an ectopic pregnancy does occur when a fertilised ovum does implant outside the normal uterine cavity
- Ectopic pregnancy is a common cause of morbidity and occasionally of mortality in women who are of reproductive age.
- It has been pointed out that the aetiology of ectopic pregnancy has remained uncertain even though a number of risk factors had been identified.
- It is known that the diagnosis of ectopic pregnancy could be difficult.
- It is known that during current practice, within developed countries, the diagnosis of ectopic pregnancy does rely upon a combination of ultrasound scanning and serial serum beta-human chorionic gonadotrophin (β-HCG) measurements.
- It is well known that ectopic pregnancy is one of the few medical conditions which can be managed by various options including expectant management, medical management, or surgical management

- Within the developed countries of the world, between 1% and 2% of all reported pregnancies have tended to ectopic pregnancies, which is comparable to the incidence of spontaneous twin pregnancy.
- The incidence of ectopic pregnancy understood to be higher within the developing countries, however, specific numbers of ectopic are not known.
- It had been pointed out that even though the incidence of ectopic pregnancy within the developed world had remained relatively static over recent years, and between 1972 and 1992 there had been an estimated six-fold rise with regard to the incidence of ectopic pregnancy. This increase in the incidence of ectopic pregnancy had been attributed to three factors which include: an increase in the risk factors including: pelvic inflammatory disease and smoking in women of reproductive age, the increased utilization of assisted reproductive technology (ART) as well as increased awareness of the condition, facilitated by the development of specialised early pregnancy units (EPUs).
- With regard to Morbidity and mortality, within the United Kingdom (UK), ectopic pregnancy has been stated to remain the leading cause of pregnancy-related first trimester death which does occur in 0.35 out of 1000 ectopic pregnancies.
- Nevertheless, within the developing world it had been estimated that 10% of women who are admitted to hospital with a diagnosis of ectopic pregnancy ultimately do die from the condition.
- It has been pointed out that ectopic pregnancy is a considerable cause of maternal morbidity, which does tend to cause acute symptoms such as pelvic pain and vaginal bleeding as well as long-term problems such as infertility. …

Ehrenberg-Buchner et al. [51] made the ensuing iterations related to ectopic pregnancy:

- Ectopic pregnancy is a common condition which is associated with the immediate risk of life-threatening haemorrhage as well as subsequent risks of infertility and recurrence of ectopic pregnancy.
- Despite remarkable advances that had been made with regard to the diagnosis and treatment of ectopic pregnancy, ectopic pregnancies do account for 9% of all maternal deaths.
- Early diagnosis of ectopic pregnancy had led to the development of innovative surgical and nonsurgical options.
- The choice of treatment of treatment of ectopic pregnancy including expectant management, medical management, and surgical approaches, does tend to depend upon the location of the ectopic pregnancy, the symptoms of the ectopic pregnancy, the gestational age, and desires for future fertility.
- The goals for the management of ectopic pregnancy are to make the diagnosis of ectopic pregnancy early as well as to provide the most effective and least invasive procedure while sparing future fertility when future fertility is desired.

Lin et al. [52] made the ensuing summating iterations related to ectopic pregnancy:

- Ectopic pregnancy does tend to account for about 2% of all pregnancies and ectopic pregnancy is the commonest cause of pregnancy-related mortality in the first trimester.
- Initial evaluation of ectopic pregnancy does consist of hormonal assays and ultrasound scan (USS) of the pelvis.
- A history of pelvic pain together with an abnormal serum β human chorionic gonadotropin level should trigger an assessment for an ectopic pregnancy.
- The fallopian tube tends to be commonest location for the development of an ectopic pregnancy.
- An adnexal mass that is found to be separate from the ovary and the tubal ring sign are the most common findings of a tubal pregnancy.
- Other types of ectopic pregnancy do include interstitial ectopic pregnancy, cornual ectopic pregnancy, ovarian ectopic pregnancy, cervical ectopic pregnancy, scar ectopic pregnancy, intraabdominal ectopic pregnancy, and heterotopic ectopic pregnancy.
- Interstitial pregnancy does occur when the gestational sac does implant within the myometrial segment of the fallopian tube.
- Cornual pregnancy is a terminology that refers to the implantation of a blastocyst within the cornua of a bicornuate or septate uterus.
- An ovarian pregnancy does occur when an ovum is fertilized and is retained within the ovary.
- Cervical pregnancy does emanate from an implantation within the endocervical canal.
- With regard to a scar ectopic pregnancy, implantation does take place within the scar of a previous caesarean section.
- With regard to an intraabdominal pregnancy, implantation does occur within the intraperitoneal cavity.
- Heterotopic pregnancy does occur when an intrauterine and an extrauterine pregnancy do occur contemporaneously.
- With regard to ectopic pregnancy, a spectrum of intra- and extrauterine findings could be visualised on ultrasound scan (US) images.
- Even though many of the ultrasound scan (US) findings tend to be nonspecific by themselves, when many of them are seen, the specificity of ultrasound scan (US) in depicting an ectopic pregnancy does substantially improve.

Tulandi and Saleh. [53] made the following summations related to ectopic pregnancy:

- The first successful surgical treatment of ectopic pregnancy (EP) was reported in 1883 by Tait. Tait undertook salpingectomy on four women who had ectopic pregnancy, and they all survived, an event that was considered to be extraordinary then.
- In 1973, Shapiro and Adler reported the treatment of ectopic pregnancy through the undertaking of laparoscopy, and these days, laparoscopy is the standard surgical approach for the treatment of ectopic pregnancy.
- The key for a successful laparoscopic treatment of ectopic pregnancy relates to early diagnosis of ectopic pregnancy. Early diagnosis of ectopic pregnancy could be achieved by serial serum human chorionic gonadotropin (β-HCG) measurement and by transvaginal ultrasound examination scan examination. Once the diagnosis of ectopic pregnancy has been made, the mode of treatment could be tailored accordingly.
- The sites of ectopic implantation could be divided into tubal ectopic pregnancy and extra-tubal ectopic pregnancy.

- Tubal pregnancy could be: ampullary ectopic pregnancy, isthmic ectopic pregnancy, fimbrial ectopic pregnancy, or interstitial ectopic pregnancy.
- Extra-tubal ectopic pregnancies do include abdominal ectopic pregnancy, ovarian ectopic pregnancy, and cervical ectopic pregnancy.

Conclusions

- Extra-uterine pregnancy does account for 1.3% to 2.4% of all pregnancies.
- 90% of ectopic pregnancies do occur within the fallopian tubes, the remaining ectopic pregnancies do tend to implant upon the cervix, the ovary, the myometrium, and other sites of the body.
- Ectopic pregnancy could manifest as abdominal or pelvic pain, amenorrhea with or without vaginal bleeding in the first trimester.
- The minimum diagnostic requirement for an ectopic pregnancy is a transvaginal ultrasound scan as well as serological confirmation of pregnancy by the undertaking of serum Beta Human Chorionic Gonadotrophin levels.
- On rare occasions ectopic pregnancy may be diagnosed incidentally.
- A patient who has a ruptured ectopic pregnancy may manifest as having an acute abdominal pain, hypotension, anaemia and would therefore require urgent resuscitation, transfusion and emergency surgical operation.
- A high index of suspicion is required to diagnose ectopic pregnancy globally.
- Even though there are facilities for the undertaking of serum Beta-Human Chorionic Gonadotrophin levels as well as trans-vaginal ultrasound scan and magnetic resonance imaging (MRI) scan in most health care establishments globally; however, facilities for the undertaking of trans-vaginal ultrasound scan and for ascertain serum Beta-Human Chorionic Gonadotrophin levels tend to be lacking in some remote health care establishments in remote areas of some developing countries as well as transportation may not be easily available in such remote areas where medical practitioners may not be available but only midwives and health care support workers and nursing staff only would tend to be available.
- Some cases of unruptured ectopic pregnancy could be safely treated with utilization of methotrexate or other medicaments without embarking on the undertaking of laparoscopic or open surgical treatment.
- All health care establishments everywhere in the world should have facilities to undertake serum Beta Human Chorionic Gonadotrophin tests as well as facilities for undertaking ultrasound scan including all remove areas in all developing countries.
- It is also important for all clinicians to be aware that it is not only gynaecologists, General Practitioners, and emergency clinicians who would may encounter patients with ectopic pregnancy, but other clinicians including paediatricians, General Surgeons, and Urologists may be the first clinicians to see female patients who present with lower abdominal pain and on rare occasions some of these patients could have ectopic pregnancy and hence all clinicians need to have a high index of suspicion for ectopic pregnancy in females of reproductive age who manifest with lower abdominal pain.

Conflict of interest - None

Acknowledgements

Acknowledgements to:

- Radiology Case Reports and Elsevier for granting copyright permission for reproduction of figures and contents of their Journal article under copyright @ 2018 The Authors This is an open Access article under the CC BY-NC-ND licence (http://creativecommons.org/licences/by-nc-nd/4.0/).
- Reproductive Biology and Endocrinology. for granting copyright permission for reproduction of figures and contents of their Journal article under copyright @ The Author(s). 2016. Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International Licence (http://creativecommons.org/licences/by-nc-nd/4.0/), which permits unrestricted use, distribution, and reproduction, in any medium, provided you give appropriate credit to the original author(s), and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver. (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

References

1. Gari R, Abdulgader R, Abdulqader O. (2020)A Live 13 Weeks Ruptured Ectopic Pregnancy: A Case Report. Cureus. Oct 16;12(10):e10993
2. Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 191: Tubal Ectopic Pregnancy. Obstet Gynecol. Feb;131(2): e65-e77.
3. Taran FA, Kagan KO, Hübner M, Hoopmann M, Wallwiener D, Brucker S. (2015) The Diagnosis and Treatment of Ectopic Pregnancy. Dtsch Arztebl Int. Oct 9;112(41):693-703; quiz 704-705.
4. Panelli DM, Phillips CH, Brady PC. (2015)Incidence, diagnosis and management of tubal and nontubal ectopic pregnancies: a review. Fertil Res Pract. Oct 15; 1:15.
5. Belics Z, Gérecz B, Csákány MG. A(2014) méhen kívüli fogamzás korai diagnosztikája [Early diagnosis of ectopic pregnancy]. Orv Hetil. Jul 20;155(29):1158-66. Hungarian
6. ZiadieMS. (2022). Ectopic pregnancy. PathologyOutlines.com website.Accessed October 9th
7. Sorelle N, Chang R, Chen H. (1995) Ectopic / tubal pregnancy. PathologyOutlines.com website. Centers for Disease Control and Prevention (CDC). Ectopic pregnancy--United States, 1990-1992. MMWR Morb Mortal Wkly Rep. Jan 27;44(3):46-48. PMID: 7823895.
8. Centers for Disease Control and Prevention (CDC). Ectopic pregnancy--United States, 1990-1992. MMWR Morb Mortal Wkly Rep. 1995 Jan 27;44(3):46-48. PMID: 7823895.
9. Creanga AA, Syverson C, Seed K, Callaghan WM. (2017)Pregnancy-Related Mortality in the United States, 2011-2013. Obstet Gynecol. Aug;130(2):366-373.
10. Tao G, Patel C, Hoover KW. (2017) Updated Estimates of Ectopic Pregnancy among Commercially and Medicaid-Insured Women in the United States, 2002-2013. South Med J. Jan;110(1):18-24.
11. Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. (2002) Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. Hum Reprod. Dec;17(12):3224-3230.

12. Chukus A, Tirada N, Restrepo R, Reddy NI. Uncommon Implantation Sites of Ectopic Pregnancy: Thinking beyond the Complex Adnexal Mass. Radiographics. 2015 May-Jun;35(3):946-959
13. Dziedzic JM, Patel PV. (2019) Cervical Ectopic Pregnancy: A Rare Site of Implantation. J Emerg Med. Jun;56(6):e123-e125.
14. Karpathiou G, Kassir R, Berremila SA, Camy F, Peoc'h M. (2018)Liver ectopic pregnancy complicating a focal nodular hyperplasia. Pathology. 2018 Jun;50(4):478-479.
15. Greenbaum A, Miskimins R, Coffman B, Paul (2016) J. Management of splenic ectopic pregnancy presenting with massive haemoperitoneum. BMJ Case Rep. Dec 8; 2016: bcr2016218291.
16. ash YH, Habash MY. (2020) Ectopic pregnancies in caesarean section scars: 5 years experience. Clin Imaging. Oct; 66:26-34.
17. Tang W, Mao J, Li KT, Walker JS, Chou R, Fu R, Chen W, (2020) Darville T, Klausner J, Tucker JD. Pregnancy and fertility-related adverse outcomes associated with Chlamydia trachomatis infection: a global systematic review and meta-analysis. Sex Transm Infect. Aug;96(5):322-329.
18. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM. (1996)Risk factors for ectopic pregnancy: a meta-analysis. Fertil Steril. Jun;65(6):1093-9. PMID: 8641479.
19. Marion LL, Meeks GR. (2012) Ectopic pregnancy: History, incidence, epidemiology, and risk factors. Clin Obstet Gynecol. Jun;55(2):376-386.
20. Yang C, Cai J, Geng Y, Gao Y. (2017) Multiple-dose and double-dose versus single-dose administration of methotrexate for the treatment of ectopic pregnancy: a systematic review and meta-analysis. Reprod Biomed Online. Apr;34(4):383-391
21. Brancazio S, Saramago I, Goodnight W.(2019) McGinty K. Cesarean scar ectopic pregnancy: Case report☆. Radiol Case RepFeb 2;14(3):354-359.
22. Fylstra DL. (2012) Ectopic pregnancy not within the (distal) fallopian tube: etiology, diagnosis, and treatment. Am J Obstet Gynecol. Apr;206(4):289-299.
23. Rosen T. (2008) Placenta accreta and cesarean scar pregnancy: overlooked costs of the rising cesarean section rate. Clin Perinatol. Sep;35(3):519-529, x.
24. Rotas, M.A., Haberman, S. and Levgur, M. (2006); Cesarean Scar Ectopic Pregnancies: Etiology, Diagnosis and Management. Obstetrics & Gynecology, 107, 1373-1377.
25. Cömert E.H., Şal H., Ekici Y.S., Seda E., Guven G. (2018); Cesarean scar pregnancy: a case report. Turkiye Klinikleri Jinekoloji Obstetrik. 26(1):37–39
26. Patel M.A. (2015);Scar ectopic pregnancy. J Med Biol Eng. 65(6):372–375.
27. Vial Y, Petignat P, Hohlfeld (2000) P. Pregnancy in a cesarean scar. Ultrasound Obstet Gynecol. Nov;16(6):592-593.
28. Timor-Tritsch IE, Monteagudo A, Cali G, El Refaey H, Kaelin Agten A, Arslan AA.(2016) Easy sonographic differential diagnosis between intrauterine pregnancy and cesarean delivery scar pregnancy in the early first trimester. Am J Obstet Gynecol. Aug;215(2): 225.e1-7.
29. Kaelin Agten A, Cali G, Monteagudo A, Oviedo J, Ramos J, Timor-Tritsch I. The clinical outcome of cesarean scar pregnancies implanted "on the scar" versus "in the niche". Am J Obstet Gynecol. 2017 May;216(5): 510.e1-510.e6.
30. El-sayed El-badawy A., El-agwany S.A., El-habashy M.A., Elmansy(2015); A. Lower uterine segment pregnancy (Cesarean Scar Pregnancy and early placenta accreta: a rising complication from cesarean section with possible and similar early ultrasound diagnoses and management. Egypt J Radiol Nucl Med. 46(4):977–980
31. Peng KW, Lei Z, Xiao TH, Jia FG, Zhong WX, Gao Y, Shen BX, Xie JW. (2014)First trimester caesarean scar ectopic pregnancy evaluation using MRI. Clinical radiology. Feb 1;69(2):123-129.
32. Godin PA, Bassil S, Donnez J. (1997)An ectopic pregnancy developing in a previous caesarian section scar. Fertility and sterility. Feb 1;67(2):398-400.
33. Fylstra DL, Pound-Chang T, Miller MG, Cooper A, Miller KM. Ectopic pregnancy within a cesarean delivery scar: a case report. American journal of obstetrics and gynecology. 2002 Aug 1;187(2):302-304.
34. Alkatout I, Honemeyer U, Strauss A, Tinelli A, Malvasi A, Jonat W, Mettler L, Schollmeyer T. (2013) Clinical diagnosis and treatment of ectopic pregnancy. Obstetrical & gynecological survey. Aug 1;68(8):571-581.
35. Yoder N, Tal R, Martin JR. (2016) Abdominal ectopic pregnancy after in vitro fertilization and single embryo transfer: a case report and systematic review. Reprod Biol Endocrinol. Oct 19;14(1):69.
36. Khalil MM, Badran EY, Ramadan MF, Shazly SA, Ali MK, Badee AY. (2012) An advanced second trimester tubal pregnancy: Case report. Middle East Fertility Society Journal. Jun 1;17(2):136-
37. Gueye MD, Gueye M, Thiam I, Mbaye M, Gaye AM, Diouf AA, Niang MM, Moreau JC. (2013) Unruptured tubal pregnancy in the second trimester. South Sudan Medical Journal.6(4):95-96.
38. Santos L T R, Oliveira S C S, Rocha L G A, Sousa N D S, Figueiredo R S. (2020) Interstitial Pregnancy: Case Report of Atypical Ectopic Pregnancy. Cureus. May 13;12(5): e8081.
39. Green LK, Kott ML. Histopathologic findings in ectopic tubal pregnancy. Int J Gynecol Pathol. 1989;8(3):255-262.
40. Saraçoglu FO, Mungan T, Tanzer F. (1992) Salpingitis isthmica nodosa in infertility and ectopic pregnancy. Gynecol Obstet Invest.34(4):202-205.
41. Majmudar B, Henderson PH 3rd, Semple E. (1983) Salpingitis isthmica nodosa: a high-risk factor for tubal pregnancy. Obstet Gynecol. Jul;62(1):73-78. PMID: 6856228.
42. Lurie S, Katz Z, Yechezkeli Y, Lifscitz-Mercer B, Shoham Z. (1994) Microscopic salpingitis is not an etiologic factor of tubal pregnancy with intrauterine devices. Int J Fertil Menopausal Stud. Nov-Dec;39(6):333-336. PMID: 7889086.
43. Gayer ML, Henry-Suchet J. (1990) Contraception et stérilité tubaire d'origine infectieuse [Contraception and tubal sterility of infective origin]. J Gynecol Obstet Biol Reprod (Paris).19(2):155-164. French. PMID: 2324437.
44. Honore LH. (1978) Salpingitis isthmica nodosa in female infertility and ectopic tubal pregnancy. Fertil Steril. Feb;29(2):164-168. PMID: 624420.
45. Bolaji II, Oktaba M, Mohee K, Sze KY. (2015) An odyssey through salpingitis isthmica nodosa. Eur J Obstet Gynecol Reprod Biol. Jan;18(4):73-79.
46. Russell JB. The etiology of ectopic pregnancy.(1987) Clin Obstet Gynecol. Mar;30(1):181-190.
47. DeCherney AH, Jones EE. (1985) Ectopic pregnancy. Clin Obstet Gynecol. Jun;28(2):365-374.
48. Tempfer CB, Dogan A, Tischoff I, Hilal Z, Rezniczek GA. (2019) Chronic ectopic pregnancy: case report and systematic review of the literature. Arch Gynecol Obstet. Sep;300(3):651-660.
49. Murray H, Baakdah H, Bardell T, Tulandi T. (2005) Diagnosis and treatment of ectopic pregnancy. CMAJ October 11; 173 (8) 905-912

50. Sivalingam VN, Duncan WC, Kirk E, Shephard LA, Horne AW. (2011) Diagnosis and management of ectopic pregnancy. J Fam Plann Reprod Health Care. Oct;37(4):231-240.
51. Ehrenberg-Buchner S, Sandadi S, Moawad NS, Pinkerton JS, Hurd WW. (2009) Ectopic pregnancy: role of laparoscopic treatment. Clin Obstet Gynecol. Sep;52(3):372-379.
52. Lin EP, Bhatt S, Dogra VS. (2008) Diagnostic clues to ectopic pregnancy. Radiographics. Oct;28(6):1661-1671.
53. Tulandi T, Saleh A. (1999) Surgical management of ectopic pregnancy. Clin Obstet Gynecol. Mar;42(1):31-8; quiz 55-56.

DOI: 10.31579/2642-9756/141