

## Issues in Management of Acute Appendicitis in Pregnancy

Sivalingam Nalliah<sup>1</sup>, Lionel Wijesuriya<sup>2</sup>, Subramani Venugopal<sup>3</sup>

Acute appendicitis is an infrequent yet the commonest surgical emergency in pregnancy occurring in about 1:1500 pregnancies. The classical abdominal pain in the right lower quadrant of the abdomen is the only reliable clinical sign. Delay in diagnosis is attributed to presence of symptoms commonly seen in pregnancy like nausea and vomiting and difficulty in localizing abdominal pain due to displacement of the appendix with advancing gestation. Perforated appendix and generalized peritonitis impacts adversely on pregnancy contributing to increases in miscarriage, pre-term delivery, fetal loss and even maternal mortality. Imaging studies like abdominal ultrasonogram, helical computerized tomography and magnetic imaging have been utilized to complement clinical suspicion and decrease 'negative appendectomies' but robust data on their routine use is awaited. Although the laparoscopic approach is a useful diagnostic and therapeutic tool in early pregnancy, its use as the primary approach for appendectomy in pregnancy requires further evaluation as increases in the incidence of fetal loss of 5.6% has been reported compared to 3.1% in open access surgery.

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### Introduction

Acute appendicitis is an infrequent yet the commonest surgical emergency encountered in pregnancy occurring in about 1:1500 pregnancies<sup>1</sup>. The clinical diagnosis, though not unlike that in the non-pregnant woman, can be difficult particularly with advancing pregnancy. Delay in diagnosis may lead to perforation which carries high morbidity in pregnancy. Mortality in pregnancy ranges from 1-5% depending on the clinical state at the point of diagnosis with perforation and generalized peritonitis carrying the highest rate<sup>2,3,4</sup>.

Issues in diagnosis in relation to patho-physiology merit discussion especially with the advent newer imaging studies.

Re-visiting current controversies surrounding surgical approaches and treatment modalities would increase the need for counseling afflicted patients.

### Pathogenesis

Obstruction of the appendicular lumen is implicated through submucosal lymphoid follicle hyperplasia following infection. Although parasitic infestation may initiate the process, it is not a common etiology in adults. Faecolith or foreign body is also implicated. Whatever the source of obstruction, intraluminal pressure increases with continued mucosal secretion and bacterial infection causing lymphatic and venous obstruction culminating in oedema and congestion of the inflamed appendix. If the condition is not treated at this stage, further increases in intraluminal pressure would compromise arterial blood flow culminating in infection and gangrene. Perforation of the appendix is likely with invasion of the serosa as necrosis of the appendicular wall is inevitable. Perinatal mortality is said to be around 35% in the presence of perforation<sup>2</sup>. Anderson *et al.* noted that perforation in pregnancy varied with gestational age approximating 6% in the first trimester, 10% in second and 13 % in the third trimester<sup>5</sup>.

Incidental findings of endometriosis of the appendix, adenocarcinoma (secondary to pelvic tumors) and tuberculosis of the peritoneum have been reported in the literature<sup>6,7</sup>.

### Peculiarities of appendicitis in pregnancy

The vermiform appendix is usually located in the right iliac fossa during the first trimester when the pregnancy is still in the pelvis. In the early stages of the disease, pain in the right iliac fossa is classically described and remains the most reliable symptom in pregnancy.

<sup>1</sup>Department of Obstetrics and Gynecology, International Medical University, MALAYSIA

<sup>2</sup>Department of Surgery, International Medical University, MALAYSIA

<sup>3</sup>Department of Imaging and Radiology, Tuanku Jaafar Hospital, Seremban, MALAYSIA

*Address for Correspondence:*

Professor Dato' Dr Sivalingam Nalliah, Department of Obstetrics and Gynecology, International Medical University, Jalan Rasah, 70300 Seremban, MALAYSIA

Email: sivalingam\_nalliah@imu.edu.my

Visceral pain manifested as epigastric or periumbilical pain is noted in the early phase of obstruction of the infected appendix irrespective of its anatomical position. In the later gestational weeks, as the abdominal wall is distended, the anterior abdominal wall is distanced from the inflamed appendix losing the ability of the mother to demonstrate guarding and rigidity, two valuable signs of acute appendicitis. Generalized peritonitis is manifested by generalized guarding of the abdomen. Nausea and vomiting can be accompanying symptoms. Hence a great deal of care needs to be taken to make a diagnosis as clinical examination can vary a great deal making accurate diagnosis difficult<sup>4</sup>. Clearly, gestational age impacts on both symptoms and signs. However, with increasing luminal size of the appendix due to serosal secretion and pus collection, the overlying parietal peritoneum is irritated causing local pain and tenderness. The gestational size of the uterus displaces the appendix including the caecum (if it is mobile) resulting in the pain being localized away from the right lower quadrant. As the pregnant uterus ascends into the abdomen,

the appendix is believed to be displaced upwards and laterally so that the tip may be close to the right flank in late second trimester. This displacement further presents diagnostic difficulties. Acute pyelonephritis and even surgical causes of right hypochondrial pain will be included in the differential diagnosis (Table 1).

The upward and lateral displacement of the appendix adversely affects the omentum from effectively walling off and containing the inflamed appendix and may contribute to a higher risk of unchecked inflammatory spread and peritonitis. Perforated appendix was seen in 30% of appendicitis during pregnancy in one large series<sup>8</sup>.

Atypical presentation, rarely due to a pelvic appendix, displacement of the appendix by the growing uterus and the pathogenesis favoring ease of spread of infection into the peritoneum contribute to delay in diagnosis and contribute to increased morbidity (and mortality) to both mother and fetus.

**Table I : Differential Diagnosis Acute Abdomen in Pregnancy**

<b>1. Pregnancy Related</b>	
Intrauterine pregnancy	Associated gynecological conditions
Miscarriage	Ovarian tumor 'accident' (rupture, torsion)
1 <sup>st</sup> trimester(Complete, Incomplete, Septic)	Corpus luteal hemorrhage
2 <sup>nd</sup> Trimester (pre-term labor, abruption placenta, rupture of uterus)	Red degeneration of leiomyoma
Extra uterine pregnancy	Pelvic abscess
Tubal ectopic pregnancy	Rupture of endometrioma
Abdominal pregnancy	
<b>2. Non-Pregnancy Related</b>	
Acute appendicitis	Tuberculosis of cecum/peritoneum
Intestinal obstruction	Acute pyelonephritis
Caecal tumor	Surgical causes of right hypochondrium

### Differential diagnosis

Delay in diagnosis is related to difficulties in interpreting signs and symptoms; nausea and vomiting are two complaints common in early pregnancy. Lower abdominal crampy pain is seen in preterm contractions, localized abdominal pain can be present in abruption placenta, and loin pain accompanied by vomiting are common in acute pyelonephritis.

Apart from the obstetric and surgical causes of abdominal pain of RIF, right loin and right hypochondrium mentioned above, gynecological disorders need consideration in the differential diagnosis. Degenerating leiomyoma, ovarian tumor accidents (torsion being the commonest), hyperstimulated ovarian syndrome, ruptured corpus luteal cyst in pregnancy and the uncommon co-existing tubal ectopic pregnancy are conditions to be considered.

Difficulty in diagnosis is further compounded by abdominal pain in pregnancy being less classical than in the non-pregnant state. Fever, nausea and vomiting, pus cells on urine analysis and leucocytosis all lack sensitivity and specificity. As mentioned above, nausea and vomiting are seen as part of the symptoms of early pregnancy.

Clinical sense and maintaining a high degree of suspicion through close observation and repeated clinical reviews remains the mainstay of establishing the diagnosis. Ancillary imaging tests have not been routinely instituted as positive predictive values depend on state of the pathology and clinical experience. However, they are becoming more relevant in reducing the high percentage of negative appendectomies following clinical diagnosis made in error. Negative appendectomies rates vary from 18% to 27%<sup>8</sup>.

### Value of imaging in diagnosing appendicitis in pregnancy

Clinical diagnosis remains the common mode. Imaging

methods, though worthy of discussion should not be awaited if delay in obtaining the service is anticipated as such delay in surgical intervention may not be wise in pregnancy in view of increased fetal and maternal morbidity and mortality. Fetal loss of 4-6 % and early delivery rates of 10-11% have been reported<sup>8</sup>.

Antiquity reliance on history and diagnostic difficulties in eliciting physical signs based on the anatomical displacement of the appendix with increasing gestational age is reiterated. Imaging studies and expertise in interpretation may not be forthcoming in centers with resource limitations and are not among the recommended routine especially when clinical assessment skews to a clear diagnosis of appendicitis.

### Currently available imaging tools

Although currently employed imaging tools have limitations its complementary use may be useful if it contributes to reduction in negative appendectomies. Some of the commonly used imaging tools are discussed below.

#### i. Plain radiography:

Although a plain radiograph may show dilated sentinel loop of bowel and air-fluid levels in the right lower quadrant it may not be advisable in pregnancy as the sensitivity and specificity are low and cannot be justified on a risk-benefit basis in pregnancy, especially in the first trimester. Where intestinal obstruction is considered as a possibility warranting plain radiographs, single exposure after obtaining informed consent may be necessary before surgical intervention<sup>9</sup>.

#### ii. Ultrasonography

Two-D ultrasonography has been used to evaluate gynecologic pathology. However, it has not been popular in imaging the gut because gas filled bowels are a poor medium for insonation. More recently ultrasonography has been shown to reduce the percentage of negative

appendectomies. Graded compression displaces bowel loops away from the area of interrogation facilitating better evaluation. Good results in ultrasonic diagnosis have been reported by Eryimaz *et al.*<sup>10</sup>.

When the appendix is inflamed the lumen is distended and non-compressible and the diameter exceeds 6 mm, distinguishing it from the neighboring gas-filled caecum. The blind ended distended appendix will appear as a non-peristaltic loop of bowel (close to the caecum). Additional aids include periappendiceal fluid and at times 'thickening of the caecum'<sup>11</sup>.

The size of the uterus (related to the gestational age) and the site of abdominal pain may assist the ultrasonographer to direct the area of concern to determine the cause of pain. Whilst this imaging modality carries no risk in pregnancy, it will also be a useful adjunct in excluding other causes of acute pain in the lower right quadrant of the abdomen e.g. tubal ectopic pregnancy, red degeneration of leiomyoma, adnexal masses, pus in the pelvis; apart from affording an opportunity to determine fetal age and viability. The kidneys, liver and gallbladder could also be imaged at the same sitting making abdominal ultrasonography a useful diagnostic tool in pregnancy. Sensitivity and specificity exceeding 85% has been reported<sup>11,12,13</sup>.

### iii. Computed tomography and Magnetic Resonance Imaging

The use of helical CT has been valuable in improving accuracy of diagnosis. Typically the inflamed swollen appendix is well seen with a thickened wall and peri-appendiceal fat stranding. Peri-appendiceal fluid, fecolith and worms can be detected. The CT also throws light on other surgical and gynecologic pathology which are included in the differential diagnosis. Castro *et al.* conclude that CT imaging is more sensitive and is preferred to ultrasonography<sup>14</sup>. Fuchs *et al.* alluded to marked reduction of negative appendectomies to less than 5% in women using CT<sup>15</sup>.

Concerns about radiation during CT imaging limit its extensive use in pregnancy. In obstetric practice, there must be clear indications before requesting for CT scans in pregnancy especially in the first trimester as the pregnant uterus remains in the true pelvis till 12 weeks gestation. A practical alternative in the first trimester would be a diagnostic laparoscopy in indicated cases. This surgical approach has the added advantage of accurate diagnosis of pelvic pathology apart from acute appendicitis, following a preliminary evaluation using ultrasonography.

### iv. CT-ultrasonography

A combination of ultrasonography followed by CT scanning improves accuracy of diagnosis in a step ladder fashion. Advocates argue that fetal morbidity has to be contended with in the event of negative appendectomies and more sensitive tools like Ultrasound-CT would have benefits. Again, a risk-benefit analysis for the use of radiation in pregnancy has to be considered.

### v. Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a more expensive tool and presents some discomfort especially in late pregnancy as mothers have to endure the procedure within an enclosed space. The advantage of safety in pregnancy makes it a better choice compared to CT, granted patient acceptability, availability and cost-benefit in appendicitis in pregnancy. As was mentioned under CT images, MRI contributes to accurate diagnosis when multiple pathology is considered in acute abdomen in pregnancy.

In view of cost, availability and unknown biological risks, MRI may be considered only in cases where prior ultrasonography and clinical findings have been equivocal and a negative appendectomy is to be avoided to avoid adverse effects on the pregnancy.

In a retrospective evaluation of 86 patients admitted with 'acute appendicitis' between 1997-2006, negative appendectomy was evaluated by Wallace *et al.*<sup>16</sup>.

Clinical evaluation alone led to 54% (7/13) negative appendectomies as opposed to 36% (20/55) with the use of ultrasonography and 8% (1/13) with ultrasonography followed by CT. The significant reduction of negative appendectomy with US & CT ( $p < 0.05$ ) was not seen with clinical evaluation alone or with the use of ultrasonography.

Radiation from imaging is of concern in obtaining informed consent for selected imaging techniques (eg. CT). Radiation dose from MDCT during early gestation has been found to be below that thought to induce neurological detriment (1.52-1.68 cGy for imaging appendix in pregnancy). However, there is a theoretical risk of doubling the fetal risk of developing childhood cancer following imaging the mother<sup>17</sup>.

As there appears to be great variance in the usage of modalities in the diagnosis of appendicitis in pregnancy, Jaffe *et al.*<sup>18</sup> evaluated the practice pattern among 183 radiology residents' program in the USA. Eighty five (46%) of the surveys were returned for evaluation. Eighty two (82/85) performed CT in pregnancy when benefit outweighed risks. Of these, 58/85 (68%) obtained informed consent. Eighty (94%) did MRI with 43% obtaining informed consent. Fifty seven (67%) did not give gadolinium in pregnancy. The CT was preferred to MRI in second and third trimester (58% vs. 29%). The MRI was preferred in the first trimester and when pelvic abscess was suspected (46% vs. 32%).

### Issues in Clinical Management

Early and accurate diagnosis of acute appendicitis warrants urgent surgical intervention. The gestational age and the clinical state of the patient are of primary concern. Perforated appendicitis with generalized peritonitis carries the risk of wound infection and complications related to peritonitis. The perinatal outcome is frequently poor with spontaneous miscarriage, fetal loss and preterm labor being common sequelae. Mazze & Kallen<sup>1</sup>, quoting from their series of 778 cases, noted a positive diagnosis in 60-70%, with accuracy being inversely proportionate to gestational

age. Seventy-seven per cent accuracy was seen when patients presented in the first trimester. This figure fell to 57% when the disease occurred in the second and third trimester. This is understandable for the reasons mentioned above about displacement of the appendix with increasing gestation.

The team approach to management with involvement of obstetricians, pediatricians, surgeons and intensivists is vital. The use of dexamethazone for fetal lung maturity is relevant between 22-36 weeks gestation with facilities for caring of the pre-term baby should the need arise<sup>19</sup>.

The surgical incision made at open access surgery if laparotomy is elected for, is determined by the gestational age and ease of access to the appendix. Transverse, midline, McBurneys, and Lanz, etc incisions have been described. By convention, the incision should be such that appendectomy is facilitated together with ability to perform peritoneal toilet in indicated cases with minimal manipulation of the pregnant uterus. The benefits of minimal access surgery are well known (especially if diagnostic laparoscopy is indicated).

Laparoscopic surgery has been in vogue and has been propagated because of early ambulation and short post-operative recovery period<sup>20,21</sup>.

There have been concerns about the ill-effects of carbon dioxide during creation of pneumoperitoneum leading to fetal hypercapnia and acidosis in animal studies<sup>22</sup>. To overcome such adverse effects pneumoperitoneum pressures not exceeding 12 mm Hg have been suggested<sup>23</sup>.

Some concerns have been expressed with the laparoscopic access in later pregnancy especially in the second and third trimester. Carver *et al.*<sup>24</sup> reported a small series of 28 patients with no difference with either surgical technique in the first and second trimester. However, there were two fetal losses in the laparoscopy group. Reedy *et al.* did not find any difference in perinatal outcome between laparoscopy and laparotomy (2000 cases vs. 1500 cases before 20 weeks gestation)<sup>24</sup>. A systematic analysis by Walsh *et al.*<sup>20</sup> comparing laparoscopic approach to open approach refers to some

more vital data that would be useful in deciding on choice of entry during surgery. Open laparoscopic approach appears to be preferred as suggested by the SAGES<sup>22</sup> when laparoscopic surgery is done with monitoring of maternal end tidal CO<sub>2</sub> monitoring to address issues related to fetal acidosis<sup>22,24</sup>. Walsh et al. did not find significant fetal loss or preterm delivery in any of the three trimesters of pregnancy following laparoscopy<sup>26</sup>. Popularization of the laparoscopic approach is supported by a significantly lower overall interruption of pregnancy rate of 11.3% compared to the open method (11.3% vs. 7.7% p<0.0068)<sup>20</sup>.

Mc Gory *et al.*<sup>6</sup> reviewed 3133 pregnant women with acute appendicitis among 94; 789 women drawn from the California Inpatient File between 1995-2002. Fetal loss and early delivery is shown in Table II below. Rate of negative appendectomy was higher in pregnant women compared to non-pregnant women (23% vs. 18%) which were not significant. Fetal loss was higher with complicated appendicitis (complex). The current approach to appendicitis in pregnancy puts them at 2 % risk of fetal loss even though the appendix is normal.

**Table II**

Appendectomy			
	Complex (%)	Simple (%)	Negative (%)
Fetal Loss	6	2	4
Early delivery	11	4	10

Ref (8): Mc Gory ML, Zingmond DS, Tllou A *et al.* J Am Coll Surg 2007; 205(4):534-40.

Controversy reigns about the value of laparoscopic approach compared to open access surgery as the former is apparently associated with higher fetal loss of 5.6% (35/624, significantly higher than compared to open

access surgery (3.1%, 128/4193 p<0.001), although there was a higher rate of negative appendectomies in the laparoscopic group<sup>20</sup> (Table III).

**Table III : Outcomes following Laparoscopic vs Open Appendectomy in Pregnancy**

Outcome	Laparoscopy N=624	Open Access Surgery N=4193	p
Fetal loss	5.6 % (N=35)	3.1 % (N=128)	<0.001
Preterm Labor	2.1 % (N=13)	8.1% (N=346)	<0.001
Total pregnancy Interruption	7.7 % (N=48)	11.3% (N=474)	<0.0068

Ref. (20) Walsh CA, Tjun Tang, Walsh SR Laparoscopic versus open appendectomy in pregnancy: A systematic review

Such data would have an impact on surgical choice in abdominal entry unless diagnostic laparoscopy was initially indicated in diagnostic difficulties (e.g. suspected ectopic pregnancy) to determine the cause of acute abdomen and appendicitis was discovered incidentally. Though acute appendicitis is more common in first and second trimester, perforation is more common in the third trimester necessitating a muscle splitting operation<sup>25</sup>. The increased risk of fetal loss and pre-term deliveries after surgery requires adequate counseling and obtaining informed consent for both imaging studies involving radiation and the type of surgical approach proposed for appendectomy.

Clinical optimization is imperative especially in the presence of disseminated infection (generalized peritonitis). Adequate fluid replacement and optimization of electrolytes prior to surgery would reduce metabolic complications.

Conventional teaching alludes to a combination of antimicrobials against both gram positive and gram negative organisms, but that which are friendly for use in pregnancy, is preferred as wound infection and septicemia are poorly tolerated by both mother and the fetus. A third generation cephalosporin with metronidazole or clindamycin (first trimester) would be appropriate. Long term antimicrobials are preferably continued till the patient remains afebrile for at least 48 hours after surgery completing about five days of treatment especially when there is a perforated appendix and peritonitis.

Use of prophylactic tocolysis for advanced pregnancy is controversial. No significant difference was found in its use in the laparoscopic group<sup>20</sup>. The general rule of thumb of initiating tocolysis to ensure adequate time for dexamethazone to act (for lung maturity in pre-term fetus) and possible transfer for intensive care of the neonate is usually followed only if the clinical situation permits delay in surgical intervention.

### Fetal Monitoring

In view of the perceived risk of fetal loss and pre-term labor, fetal monitoring before and after surgery especially in later gestational age, can be re-assuring to both the mother and the care-giver. Continued fetal surveillance for the next few days after surgery will direct care givers to the need for receiving a premature fetus or address management of a miscarriage. The routines of effective pregnancy care are recommended if there are no complications post-operatively and pregnancy progresses without event.

### Conclusions

Appendicitis is not a common surgical complication and diagnosis can be difficult. Fetal morbidity and mortality are high in the presence of perforation and generalized peritonitis. Diagnostic difficulties arise because of displacement of the vermiform appendix with advancing pregnancy. Judicious use of various imaging modalities may reduce 'negative' appendectomies but until favorable positive predictive values are obtained, a high clinical suspicion has to be relied upon. Open surgery appears to be preferred to laparoscopic approaches especially if a diagnostic procedure was not the initial indication unless results of a large randomized trial favor the laparoscopic method. Perioperative antibiotics are frequently administered to reduce surgical morbidity.

#### REFERENCES

1. Mazze RI & Kallen B. Appendicitis in pregnancy: a Swedish Registry Study of 778 cases. *Obstet Gynecol* 1991;77:835-840.
2. Liu CD & McFadden DW. Acute Abdomen and appendix In: Greenfield LJ, Mulholland MW, Oldham KT, editors; *Surgery: Scientific Principles and Practice*, 2<sup>nd</sup> edition Philadelphia: Lippincott, Williams & Wilkins; 1997; pp 1246-61.
3. Tamir IL, Bongard FS & Klien SR. Acute appendicitis in the pregnant patient *Am J Surg* 1990; 160:571-576.
4. Witlin AG & Sibai BM. When a pregnant patient develops appendicitis. *Contemp Obstet Gynecol* 1996; 41:15-30.
5. Andersson RE & Lambe M. Incidence of appendicitis during pregnancy. *Int J Epidemiology* 2001; 30:1281-5.
6. Faucheron JL, Pasquier D & Voin D. Endometriosis of the vermiform appendix as an exceptional cause of perforated appendectomy during pregnancy *Colorectal Dis* 2007; Dec 7 Epub ahead of publication.

7. Uohara JK & Kovra TY. Endometriosis of the Appendix: Report of 12 cases and review of literature *Am J Obstet Gynecol* 1975; 12(3):423-26.
8. Mc Gory ML, Zingmond DS, Tllou A *et al.* *J Am Coll Surg* 2007; 205(4):534-40.
9. Bimbau BA & Wilson SR. Appendicitis in the millennium *Radiology* 2000; 215(2):35-40.
10. Eryilmaz R, Sahin M, Bas G *et al.* Acute appendicitis during pregnancy *Dig Surg* 2002; 19:40.
11. Old JL, Dusing RW, Yap W *et al.* Imaging of suspected appendicitis. *Am Fam Physician* 2005;7(1):71-78.
12. Zielke A, Hasse C, Sitter H *et al.* Influence of ultrasound on clinical decision making in acute appendicitis: A prospective study *Eur J Surg* 1998;164(3):201-209.
13. Terasawa T, Blackmore CG, Bent S *et al.* A Systematic Review Computed tomography and ultrasonography to detect acute appendicitis in adults and adolescents *Ann Int Med* 2004;7;141 :537-46.
14. Castro MA, Shipp TD, Castro EE *et al.* The use of helical CT in pregnancy for diagnosis of acute appendicitis *Am J Obstet Gynecol* 2001;184:954-7.
15. Fuchs JR, Schaumberg JS, Shortsleeve MJ *et al.* Impact of abdominal CT imaging on management of appendicitis: an update. *J Surg Res* 202;106(1): 131-6.
16. Wallace CA, Petrov MS, Soybel DI *et al.* Influence of imaging on the negative appendectomy rate in pregnancy. *J Gastrointest Surg* 2008;12(1):46-50.
17. Huwitz LM, Yoshizumi T, Reiman RE *et al.* Radiation dose to fetus from MDCT during early gestation *AJR Am J Roentgen* 206;186(3):871-6.
18. Jaffe TA, Miller CM & Merie FM. Practice pattern in imaging pregnant patients with abdominal pain: a survey of academic centers. *AJR Am J Roentgenol* 2007;189(5):1128-34.
19. RCOG Guideline No. 7 Feb.2004 Antenatal Glucocorticoids to prevent Respiratory Distress Syndrome.
20. Walsh CA, Tjun Tang & Walsh SR. Laparoscopic versus open appendectomy in pregnancy: a systematic review. *Int J Surg* 2008;6:339-44.
21. Ortega AE, Hunter JG, Peters JH *et al.* A prospective randomized comparison of laparoscopic appendectomy: Laparoscopic Appendectomy Study Group. *Am J Surg* 1995;169(2):208-12.
22. Hunter JG, Swanstrom L, Thirnborg K *et al.* Carbon dioxide pneumoperitoneum induces fetal acidosis in pregnant ewe model. *Surg Endosc* 1995;9(3): 272-9.
23. Guidelines for laparoscopic surgery during pregnancy. Society of American Gastrointestinal Endoscopic Surgeons (SAGES). *Surg Endo* 1998;12 (2):189-90.
24. Carver TW, Antevil J, Eqan JC *et al.* Appendectomy during early pregnancy: what is the preferred approach. *Am J Obstet Gynecol* 2005;71(10):809-12.
25. Reedy MB, Kallen B & Kueh TJ. Laparoscopy during pregnancy: a study of fetal outcome parameters with use of the Swedish Health Registry. *Am J Obstet Gynecol* 1997;177:1539-40.
26. Grady K, Howell C, Cox C. In *Managing Obstetric Emergencies and Trauma : The MOET Course 2<sup>nd</sup> Ed.*