# Hypoxic events during non-obstetric abdominal surgery in pregnant women

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**Abstract.** – OBJECTIVE: Every year 0.5-2% of women undergo non-obstetric surgery in pregnancy. Hypoxic events with short-term and longterm consequences are one of the most frequent complications in surgery. There is only limited data available regarding the impact of these events. This review aims to analyze the current literature on hypoxic events occurring in non-obstetric abdominal surgery in pregnant women, focused on maternal and fetal outcomes.

**MATERIALS AND METHODS:** We performed a non-systematic review of the literature, through a PubMed search using the key words "hypox-emia", "non-obstetric surgery", "surgical procedures", "pregnancy", "pregnant women" and "outcome".

**RESULTS:** There is little data available regarding maternal and fetal outcomes after hypoxic episodes during non-obstetric surgery in pregnancy. In these cases, conservative intrauterine resuscitation maneuvers or immediate delivery should be taken into account. Perimortem cesarean section can be lifesaving for both mother and fetus when maternal collapse is non responsive to resuscitation procedures. Inaccurate information regarding maternal and fetal outcomes is due to the lack of robust data and the heterogeneity of the causes underlying maternal respiratory complications during surgery.

**CONCLUSIONS:** Non-obstetric surgery during pregnancy must be performed when indicated. An expert multidisciplinary team, composed of obstetricians, surgeons, and anesthesiologists need to be included, giving appropriate attention to the physiological changes of respiratory, cardiovascular, and gastrointestinal system that occur during pregnancy. The shortest operative time and peri-operative assistance should be ensured. Complications, such as hypoxic events in pregnant patients need adequate assistance. Multidisciplinary cooperation, continuous training and simulation for anesthesiology and resuscitative procedures can guarantee this. Key Words:

Hypoxia, Non-obstetric surgery, Surgical procedures, Pregnancy, Pregnant women, Outcome.

#### Introduction

The development of a normal pregnancy depends on optimal maternal health and normal placental development. Maternal exposure to hypoxic events may lead to critical injuries on fetal and maternal vital organs. There are many causes of hypoxia during pregnancy. They can be classified in preplacental, uteroplacental or postplacental. The first group includes pre-existing maternal cardiovascular conditions, maternal anemia, high-altitude, infections, maternal chronic or acute pulmonary diseases, maternal hematological disorders, and amniotic fluid embolism. Uteroplacental causes arise from abnormal placentation early in gestation and from placental vascular disease later on. Postplacental causes are related to a reduction of uterine artery flow, fetal cardiac or genetic diseases<sup>1</sup>. Among preplacental causes of hypoxia, surgery complications are included (Table I).

Every year non-obstetric surgery is performed on 0.5-2% of pregnant women<sup>2,3</sup>. These procedures include all surgeries performed throughout pregnancy, excluding fetal surgery, dilation and curettage, techniques on gestational uterus and cesarean section. The most common procedures involve abdominal surgery (appendectomy, cholecystectomy), cancer, and orthopedic surgery<sup>4</sup>. Despite the concerns which have historically been considered when operating pregnant women, due to the risk of teratogenesis, miscarriage,

Preplacental hypoxia	Uteroplacental hypoxia	Postplacental hypoxia
Pre-existing maternal cardiovascular disease	Abnormal placentation early in gestation	• Diminished uterine artery flow
Maternal chronic and acute     pulmonary disease	<ul> <li>Placental vascular disease later in pregnancy: hypertension, pre-eclampsia</li> </ul>	<ul> <li>Progressive fetal cardiac failure (congenital heart block or congenital heart malformations)</li> </ul>
<ul> <li>Maternal hematological disorders</li> <li>Amniotic fluid embolism</li> </ul>		• Important genetic fetal anomalies
<ul><li>Surgery complications</li><li>Hypoxic environment: high-altitude</li></ul>		

Table I. Causes of maternal and fetal hypoxia during pregnancy.

fetal distress, stillbirth, and preterm birth, to date it is evident that a pregnant woman should never be denied indicated surgery<sup>5</sup>.

Physiological changes on the maternal body are well known, since they expose pregnant patients to a higher risk of complications. An expert team made of anesthetists, general surgeons, and obstetrics is essential to ensure both maternal and fetal safety<sup>6</sup>. Hypoxic events are one of the most frequent complications in surgery, particularly when general anesthesia is needed. Very little data are available on the short-term and long-term impact of these complications<sup>7,8</sup>.

This review aims at analyzing the current literature on hypoxic events occurring during non-obstetric surgery on pregnant women, focused on maternal and fetal outcomes.

#### Materials and Methods

The research was done using PUBMED database up until 2019, July. All papers referring to non-obstetric surgical intervention during pregnancy were considered. A combination of Medical Subject Headings (MeSH) terms were used. The keywords used were: "hypoxia", "non-obstetric surgery", "surgical procedures", "pregnancy", "pregnant women" and "outcome". All titles and abstracts published in English were evaluated.

Each article was evaluated according to the inclusion criteria: studies reporting any non-obstetric surgical intervention under anesthesia (regional or general) during any trimester of pregnancy. All studies were considered, with the exception of those performed on animals, comments, letters, editorials, and case reports. Papers on obstetric surgery were not included. Among all the non-obstetric complications during surgery, particular attention was paid to the hypoxic one. Due to the high heterogeneity regarding the indication for surgery, surgical approach, gestational trimester, anesthesia procedures and complications, only a non-systematic review of literature and a critical synthesis of clinical experiences was performed.

The initial search yielded a total of 656 articles. Six hundred and twenty seven articles were excluded after title/abstract screening for not meeting inclusion criteria. A total of 30 articles were finally evaluated and reviewed by the authors. The selection of papers is reported in Figure 1.

#### Non-Obstetric Abdominal Surgery During Pregnancy: Indications, Planning, Techniques

The most frequent indications for non-obstetric abdominal surgery during pregnancy are acute appendicitis, cholecystitis, persistent adnexal mass, adnexal torsion, intestinal obstruction, abdominal pain of unknown etiology, cancer surgery. Maternal abdominal disease and its treatment are associated with a fetal loss rate

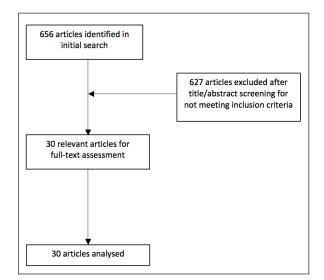


Figure 1. Flow chart for paper selection.

ranging from 2 to 24%<sup>9</sup>. Some of the causes of increased fetal morbidity during abdominal surgery include direct uterine trauma, decreased utero-placental blood flow, teratogenic effect of anesthetics, adverse effects of anesthesia on maternal hemodynamics and acid-base balance, impaired ventilatory mechanics, increased thromboembolic risk and adverse effects of postoperative medications.

Abdominal surgery during pregnancy is also related to a higher risk of maternal death. Due to the improvement of anesthesiological and surgical skills and techniques, mortality rates have dropped to a range of 0.004 to  $0.25\%^{10}$ . There are some possible explanations that justify why pregnant women have a much higher rate of postoperative complications and mortality. First, delayed diagnosis or inappropriate conservative management of surgical disease may contribute to a fatal outcome. Applying the strategy of "wait and see" may have an impact on the severity of some surgical diseases. Finally, pregnant women have a higher susceptibility to infections and postoperative septicemia. Pregnant patients undergoing surgery must receive more attention and monitoring in the peri-operative period and run the risk of long hospitalization and of being admitted into Intensive Care Unit (ICU)<sup>11</sup>.

Preoperative management includes an assessment of gestational age, the viability of the fetus and should exclude any other complications pregnancy-related. A medical history, a physical examination and informed consent need to be collected. Before surgery, intravenous crystalloids, analgesic and antibiotics must be given<sup>2</sup>.

The physiological changes that occur on maternal body during pregnancy should be considered<sup>8</sup>. The changes include cardiovascular, hemodynamic, respiratory, and gastrointestinal effects. Those occurring during the first weeks of pregnancy are driven by hormonal influence. The changes that occur later on in gestational age owe to the mechanical effect of enlarged uterus, changes in metabolic demands of the fetus and lower resistance in placental circulation<sup>6</sup>. In order to ensure a decrease in complications, the use of loco-regional anesthesia, application of airway emergency algorithms, avoidance of aorto-caval compression by left uterine displacement in later pregnancies and accurate airway protection during general anesthesia need to be encouraged<sup>6</sup>. Expert anesthesiologists are required in these cases and their continuous clinical training by simulations is recommended<sup>12</sup>.

The teratogenic action of anesthetics have been widely reported in literature. The American College of Obstetricians and Gynecologist confirmed that no currently used anesthetic drugs have demonstrated any teratogenic effects on the human fetus when using standard concentrations at any gestational age<sup>5</sup>.

There could be an increased risk of late abortion or preterm delivery during abdominal surgery. Infective agents, inflammatory conditions, as well as direct surgical stimulation of the pregnant uterine body, can cause uterine irritability and contractions. The prophylactic use of tocolytic agents is controversial and no clear benefit from routine preoperative tocolysis has been demonstrated<sup>4,9</sup>.

Laparoscopic approach is nowadays considered a safe procedure, with many advantages when compared to laparotomy. There is very little difference in the surgical outcomes of pregnant and nonpregnant patients<sup>13</sup>. Some advantages include lower risk of wound complications, less postoperative pain, shorter hospital stay, and lower thromboembolic risk due to earlier mobilization. The laparoscopic technique is preferred during the first and second trimester. During later gestational ages, there are limited data available regarding laparoscopy, because of an enlarged uterus, tissue congestion, and diminished available working space. Some authors<sup>14</sup> have demonstrated, nevertheless, that laparoscopic surgery can be safely performed up to 35 weeks. Several surgical strategies for advanced pregnancy were considered to reduce possible complications. Proper management of the trocar insertion is the most important factor able to reduce trauma to the gravid uterus and obtain adequate exposure. An open-laparoscopy technique is recommended. An ultrasonography-guided trocar insertion, in conjunction with a more cephalad trocar position may be helpful in avoiding uterine damage<sup>14</sup>. Furthermore, during laparoscopic procedures it is important to monitor maternal end-tidal pCO<sub>2</sub> to avoid fetal hypercapnia and acidosis. Low pneumoperitoneum pressures are preferable, with a maximal intra-abdominal pressure of 10-13 mmHg. Any maternal position change in a Trendelenburg or reverse Trendelenburg have to initiate slowly and reach a limited extension. It is advisable to reduce surgical time and not exceeding 90 minutes<sup>6,15-17</sup>.

No special monitoring is required in healthy patients but each case must be assessed carefully

and invasive monitoring could be required in those with severe cardiovascular or pulmonary disease<sup>18</sup>.

Postoperative management includes evaluation of fetal condition, monitoring of uterine contractility, adequate maternal analgesia and postoperative nausea-vomiting treatment. Non-steroidal anti-inflammatory drugs administered during the third trimester of pregnancy may be associated with premature closure of ductus arteriosus and possible pulmonary hypertension in the newborn in 50-80% of cases<sup>19</sup>. As pregnancy is a procoagulant state, adequate prophylaxis with heparin and pneumatic compression of the legs is advisable<sup>16</sup>.

Recommendations for proper perioperative management of pregnant women requiring surgery are summarized in Table II.

#### Hypoxic Complications: Maternal Outcome

Any approach to pregnant patients' airway system in case of surgery should be considered

difficult. Some of the causes are fluid retention, edema, hyperemia, mucosal friability, glandular hyperactivity, narrowing of the oropharyngeal diameter, and enlarged breasts. They all can result in difficult intubation.

The impairment in Functional Residual Capacity (FRC) in the supine position and increased oxygen consumption in pregnancy cause a rapid desaturation and higher risk of hypoxia during apnea. It is important to provide optimal preoxygenation without over-ventilation to avoid respiratory alkalosis<sup>20</sup>.

Failed intubation occurs eight times more commonly in pregnant patients than in others<sup>21</sup>. The incidence of hypoxaemia in case of failed intubation was much higher in this population, with greater severity and higher incidence of ICU admission<sup>22</sup>. Only in 50-66% of cases, a preoperative airway examination can identify difficult airway management<sup>23</sup>. Smaller size endotracheal tubes, laryngoscope, and video laryngoscopy must be made available. Precau-

Preoperative	<ul> <li>Appropriate medical history collection and accurate physical examination</li> <li>Obstetric evaluation: exclude any other complication related to pregnancy</li> <li>Proper indication to surgery</li> <li>Informed consent collection</li> <li>No clear benefit from routine preoperative tocolysis</li> <li>Preoperative airway examination</li> </ul>
Intraoperative	<ul> <li>Anesthesiologist</li> <li>Prefer loco-regional anesthesia (when indicated)</li> <li>Accurate airway protection during general anesthesia</li> <li>Use standard concentrations of anesthetic drugs at any gestational age</li> <li>Provide optimal preoxygenation without over-ventilation</li> <li>Monitor maternal end-tidal pCO<sub>2</sub></li> <li>Any maternal position change (Trendelenburg or reverse Trendelenburg) have to initiate slowly and reach a limited extension</li> <li>Apply airway emergency algorithms with prompt availability of advanced airway devices</li> </ul>
	<ul> <li>Surgeon</li> <li>Left uterine displacement in later pregnancies</li> <li>Laparoscopic approach is considered a safe procedure</li> <li>Prefer open access for trocar insertion</li> <li>Ultrasonography-guided trocar insertion</li> <li>More cephalad trocar position</li> <li>Apply low pneumoperitoneum pressure (maximal intra-abdominal pressure of 10-13 mmHg)</li> <li>Reduction of surgical time (not exceeding 90 minutes)</li> </ul>
Postoperative	<ul> <li>Evaluation of fetal condition</li> <li>Monitor uterine contractility</li> <li>Adequate maternal analgesia</li> <li>Adequate postoperative nausea-vomiting treatment</li> <li>Adequate prophylaxis with heparin and pneumatic compression of legs</li> <li>Adequate postoperative nausea-vomiting treatment</li> <li>Adequate prophylaxis with heparin and pneumatic compression of legs</li> </ul>

Table II. Recommendations for proper perioperative management of pregnant women requiring surgery.

tions must be taken in order to ensure an empty stomach and reduce the risk of aspiration.

When endotracheal intubation failure occurs, the "Can't Intubate, Can't Oxygenate" (CICO) and front of neck access procedures start. Surgical cricothyroidotomy and other front of neck airway techniques are required in only 1 in 60 failed intubations but, when done effectively and without delay, may be life-saving. Algorithm for the management of failed tracheal intubation during obstetric general anesthesia has been published by the Obstetric Anesthetists' Association/ Difficult Airway Society in 2015<sup>7</sup>.

The most important life-threatening risk during management of failed intubation is maternal hypoxemia. This led to immediate death in many cases, while only a few others survived with hypoxic brain damage<sup>24,25</sup>.

Other complications of airway management in pregnant women have been reported. Some of these complications are nonfatal cardiac arrest, pulmonary aspiration of stomach contents at failed intubation, rapid onset of pulmonary edema, airway trauma with mediastinitis and permanent alteration of the voice. Cardiac damage caused by hypoxia, late death, occurring more than 42 days but within the first year after delivery, have also been described after failed intubation during obstetric surgery. We found no data detailing the same risk during non-obstetric surgery in pregnant women<sup>23</sup>.

Due to the limited evidence in literature, there is no consistent demonstration that immediate delivery of a pregnant woman with respiratory failure can improve the mother's outcome. Delivery should seldom be performed in an attempt to improve maternal oxygenation and ventilation, at the expense of a premature fetus. Delivery of term fetuses can be instead beneficial for both mother and newborn in cases of intractable maternal hypoxia<sup>21</sup>.

### *Hypoxic Complication: Fetal and Neonatal Outcome*

Paucity of data are available about specific fetal and neonatal outcome after non-obstetric surgery in pregnant women. Short periods of mild hypoxemia are usually well tolerated by normal fetuses<sup>26</sup>. Nevertheless, potential for fetal hypoxia, acidosis, and even fetal death in the presence of prolonged maternal hypoxia or hypotension should be considered, since perfusion to vital maternal organs in any maternal shock state is related to the reduced uterine and fetal

perfusion<sup>6</sup>. Risk of maternal hypoxia or hypotension depends on the type of surgery and/or anesthesiological technique. In patients at high risk of maternal hypotension or hypoxia (cardiothoracic, vascular and neurosurgical procedures), a continuous fetal heart rate monitoring during surgery is generally warranted in potentially viable pregnancies<sup>4</sup>. Continuous fetal monitoring is not usually necessary during abdominal surgery, such as laparoscopic or laparotomic procedures. If intraoperative signs of fetal distress due to hypoxia are detected, non-surgical manipulation, change of patient's position, and conservative techniques for intrauterine fetal resuscitation should be taking into account. Maternal oxygenation or hemodynamic support systems can be helpful in such cases<sup>27</sup>. Emergency cesarean section is not always considered the "best" strategy, either due to potential prematurity complications in early gestational ages and due to technical difficulties in performing both cesarean section and non-obstetric surgery at the same time<sup>4</sup>.

Several reports described complications after failed intubation at cesarean section and poor neonatal outcomes due to fetal distress. There are not well-detailed studies about the neonatal outcome after hypoxic events during non-obstetric surgery in pregnant women. Based on the available data, no correlation was found between the lowest maternal oxygen saturation and Apgar score. Failed intubation and low oxygen saturation were independent predictors of neonatal ICU admission<sup>22</sup>. Actually, there was no evidence of maternal hypoxia<sup>28</sup>, extremely low maternal oxygen saturations have been related to good neonatal outcomes in other experiences<sup>22</sup>. Therefore, the maternal oxygen saturation seems not to be an accurate parameter to evaluate the fetal respiratory distress.

The most severe complication of maternal hypoxia during surgery is maternal cardiac arrest and collapse. It is a rare and acute event that involves the cardiorespiratory system and brain, followed by the reduction or absence of the level of consciousness. This definition includes events at any gestational age and up to six weeks after delivery<sup>29</sup>. There are different causes of collapse; the most common seems to be the hemorrhage, in particular postpartum hemorrhage, major antepartum hemorrhage from placenta previa/accreta, uterine rupture, ectopic pregnancy, and placenta abruption. Among other causes, there are thromboembolism, amniotic fluid embolism, cardiac disease, sepsis, drug toxicity/overdose,

eclampsia, intracranial hemorrhage, anaphylaxis, hypoglycemia, and other metabolic/electrolyte disturbances, other causes of hypoxia, such as airway obstruction secondary to aspiration/foreign body, air embolism, tension pneumothorax, cardiac tamponade secondary to trauma and hypothermia, failed intubation.

In case of an emergency, the European Resuscitation Council Guidelines for Resuscitation recommend a systematic ABCDE approach with some changes arising from the aortocaval compression of the uterus (from 20 weeks of gestation)<sup>30</sup>:

- Place the patient in the left lateral position or manually displace the uterus to the left;
- The hand position for chest compressions may need to be slightly higher on the sternum for patients with advanced pregnancy;
- Start preparing for emergency caesarean section, considered as a resuscitative procedure.

The Royal College of Obstetricians and Gynaecologists<sup>29</sup>, the European Resuscitation Council<sup>30</sup> and the American Heart Association<sup>31</sup> recommend that the perimortem caesarean section decision should be undertaken within 4 minutes of maternal collapse in the absence of response to correctly performed Cardio Pulmonary Resuscitation (CPR) and delivery should be performed within 5 minutes, regardless of gestational age. The delivery of the fetus and placenta decreases oxygen consumption, removes the impaired venous return secondary to aortocaval compression, improves the cardiac output and facilitates chest compressions and ventilation. Before 20 weeks of gestation, there is not any proven benefit from this procedure<sup>29</sup>. Accuracy about data regarding maternal and fetal outcomes are low because of the lack of robust data and the heterogeneity of the causes underlying maternal collapse<sup>29</sup>. Infant survival has been reported even when delivery was performed after 5 minutes of CPR for maternal collapse, with variable outcomes, including neurological or respiratory sequelae, retinopathy, hearing loss, and neonatal death due to complications of prematurity<sup>32</sup>.

#### Conclusions

Non-obstetric surgery during pregnancy is not an uncommon event and it must be performed when indicated. Expert multidisciplinary team, composed by obstetricians, surgeons and anesthesiologists should be involved, in order to

approach any treatment with appropriate attention to the physiological changes of respiratory, cardiovascular, and gastrointestinal system occurring in pregnancy and to ensure the shortest operative time and the correct peri-operative assistance. Several complications can occur. Difficult intubation and complications related to acute hypoxia are some of these. Scant data are available regarding maternal and fetal outcomes after hypoxic episodes during non-obstetric surgery in pregnancy. Conservative intrauterine resuscitation maneuvers or immediate delivery are relevant decisions. Each case management needs to be personalized, depending on the maternal clinical condition, the gestational age and signs of fetal hypoxia and acidosis. Perimortem cesarean section in case of maternal collapse non-responsive to resuscitation procedures can be life saving for both mother and fetus. Lower accuracy of data regarding maternal and fetal outcomes is due to causes' heterogeneity of the underlying maternal respiratory complications during surgery. Multidisciplinary approach, continuous training, and simulation for anesthesiology and resuscitative procedures can be useful to properly assist pregnant patients in case of a hypoxic emergency during surgery.

#### **Conflict of Interest**

The Authors declare that they have no conflict of interests.

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