

Non-obstetric surgery during pregnancy and the effects on maternal and fetal outcomes: A systematic review

Anna Haataja, Hannu Kokki, Outi Uimari and Merja Kokki

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Abstract

Background and objective: Non-obstetric surgery is fairly common in pregnant women. We performed a systematic review to update data on non-obstetric surgery in pregnant women. The aim of this review was to evaluate the effects of non-obstetric surgery during pregnancy on pregnancy, fetal and maternal outcomes.

Methods: A systematic literature search of MEDLINE and Scopus was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The search span was from January 2000 to November 2022. Thirty-six studies matched the inclusion criteria, and 24 publications were identified through reference mining; 60 studies were included in this review. Outcome measures were miscarriage, stillbirth, preterm birth, low birth weight, low Apgar score, and infant and maternal morbidity and mortality rates.

Results: We obtained data for 80,205 women who underwent non-obstetric surgery and data for 16,655,486 women who did not undergo surgery during pregnancy. Prevalence of non-obstetric surgery was between 0.23% and 0.74% (median 0.37%). Appendectomy was the most common procedure with median prevalence of 0.10%. Near half (43%) of the procedures were performed during the second trimester, 32% during the first trimester, and 25% during the third trimester. Half of surgeries were scheduled, and half were emergent. Laparoscopic and open techniques were used equally for abdominal cavity. Women who underwent non-obstetric surgery during pregnancy had increased rate of stillbirth (odds ratio (OR) 2.0) and preterm birth (OR 2.1) compared to women without surgery. Surgery during pregnancy did not increase rate of miscarriage (OR 1.1), low 5min Apgar scores (OR 1.1), the fetus being small for gestational age (OR 1.1) or congenital anomalies (OR 1.0).

Conclusions: The prevalence of non-obstetric surgery has decreased during last decades, but still two out of 1000 pregnant women have scheduled surgery during pregnancy. Surgery during pregnancy increases the risk of stillbirth, and preterm birth. For abdominal cavity surgery, both laparoscopic and open approaches are feasible.

Keywords

Systematic review, surgery, laparoscopy, pregnancy, trimesters, premature birth, abortion, threatened, fetal death, maternal mortality, congenital abnormalities, developmental disabilities

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Corresponding author:

Merja Kokki

Department of Anesthesia and Intensive Care Medicine
Kuopio University Hospital
PO Box 100
Kuopio FI-70029 KYS Finland
merja.kokki@kuh.fi

Anna Haataja

PEDEGO Research Unit,
Medical Research Center Oulu,
University of Oulu, Oulu,
Finland

Hannu Kokki

School of Medicine, Faculty
of Health Sciences, University
of Eastern Finland, Kuopio,
Finland

Outi Uimari

PEDEGO Research Unit,
Medical Research Center Oulu,
University of Oulu, Oulu,
Finland

Department of Obstetrics and
Gynecology, Oulu University
Hospital, Oulu, Finland

Merja Kokki

Department of Anaesthesia
and Intensive Care Medicine,
Kuopio University Hospital,
Kuopio, Finland



Context and Relevance

Previous studies demonstrate that non-obstetric surgery is common in pregnant women with the prevalence of 0.5%–2%. Emergent situations may require urgent surgical treatment, but pregnant women undergo elective surgeries also. Surgery is associated to increased risk of adverse birth outcomes, such as miscarriage, stillbirth, preterm birth, low birth weight, and a low Apgar score.

Our study indicates that the prevalence of non-obstetric surgery has decreased in recent years, but elective surgery is still common in pregnant women. Surgery during pregnancy increases the risk of stillbirth, preterm birth, and congenital anomalies. Fetal and maternal safety of non-obstetric surgery has, however, increased during the last two decades and surgical intervention should not be postponed in emergent conditions requiring surgery.

Introduction

Older data indicate that non-obstetric surgery is performed in 0.5%–2% of all pregnancies and that the most common conditions requiring surgical intervention during pregnancy are appendicitis, cholecystitis, gynecological disorders, and traumas.¹ It has been proposed that scheduled surgery should be postponed until after pregnancy,^{2,3} but both scheduled and emergent surgeries are fairly commonly performed in pregnant women. Emergent situations, such as acute appendicitis and ovarian torsion, often require urgent intervention, whereas the timing of scheduled surgery in pregnant patients must be carefully evaluated.² If scheduled surgery is required during pregnancy, the second trimester after organogenesis is considered the most appropriate time.^{1,3}

Non-obstetric surgery during pregnancy increases the risk of adverse birth outcomes, such as miscarriage, stillbirth, preterm birth, low birth weight, and a low Apgar score.^{1,4,5} Surgical disease and surgery predispose both pregnant woman and fetuses to several risks, such as surgical and oxidative stress, anesthetics, analgesics, and postoperative pain, which may also affect the course of pregnancy. Longer anesthesia duration in pregnancy may induce fetal neuronal injury and increase the risk of impaired learning and memory during childhood and adolescence.⁶ The timing of the surgery may affect the risk of adverse birth outcomes, as surgical procedures performed in the first and third trimesters are associated with a higher risk of preterm birth, birth weight under 1750 g, and low Apgar scores.^{3,7} However, the surgical condition itself can be a risk for the pregnant woman, the pregnancy outcome, and the fetus if left untreated. Therefore, surgical intervention should not be postponed if symptoms do not improve with conservative measures or if conservative measures are not available.^{1–4}

In this study, our aim was to update data on non-obstetric surgery in pregnant women. During the last two decades,

the diagnostic accuracy of surgical conditions has improved, mini-invasive surgical techniques have become more common, perioperative fetal monitoring and maternal–fetal care have improved, and updated guidelines on non-obstetric surgery during pregnancy have been published.^{2,3} Our hypothesis was that the prevalence of non-obstetric surgery has decreased, and the safety of surgery has increased during the last two decades compared to previously. In this updated systematic review, we evaluated the effects of non-obstetric surgery during pregnancy on pregnancy and fetal and maternal outcomes. In addition, the prevalence of non-obstetric surgery, the proportions of emergent and scheduled surgery, and the proportions of laparoscopic and open approaches in non-obstetric surgery in pregnant women were quantified.

Methods

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.⁸

Search strategy

A systematic literature search of MEDLINE (PubMed) and Scopus was conducted in January 2020 and updated in November 2022. The search strategy combined Medical Subject Heading (MeSH) terms and keywords. The following terms were used in combination to search for relevant studies: pregnancy outcome, preterm delivery, birth outcome, spontaneous abortion, miscarriage, live birth, stillbirth, non-obstetric, laparoscopic, surgical, surgery, and surgical procedures. The initial search was restricted to English-language articles published between January 1989 and November 2022 and produced 185 relevant results. The literature search was performed under the guidance of an information retrieval and information management professional. The search strategy is demonstrated in Appendix 1.

Study selection

Two independent reviewers (AH and HK) participated in the study selection and data extraction, and any disagreements were resolved through dialogue. In the first phase, article titles were screened for relevance, and the resulting set was reduced from 185 articles to 97. In the second phase, the abstracts were reviewed, and 51 articles were selected for further evaluation. After excluding double publications, overlapping studies, and irrelevant publications, and restricting selection to articles published between January 2000 and November 2022 to have the most up-to-date data, a total of 36 studies matched the inclusion criteria. An additional 24 citations were identified through reference mining. Ultimately, 60 studies were included in the review (Figure 1).

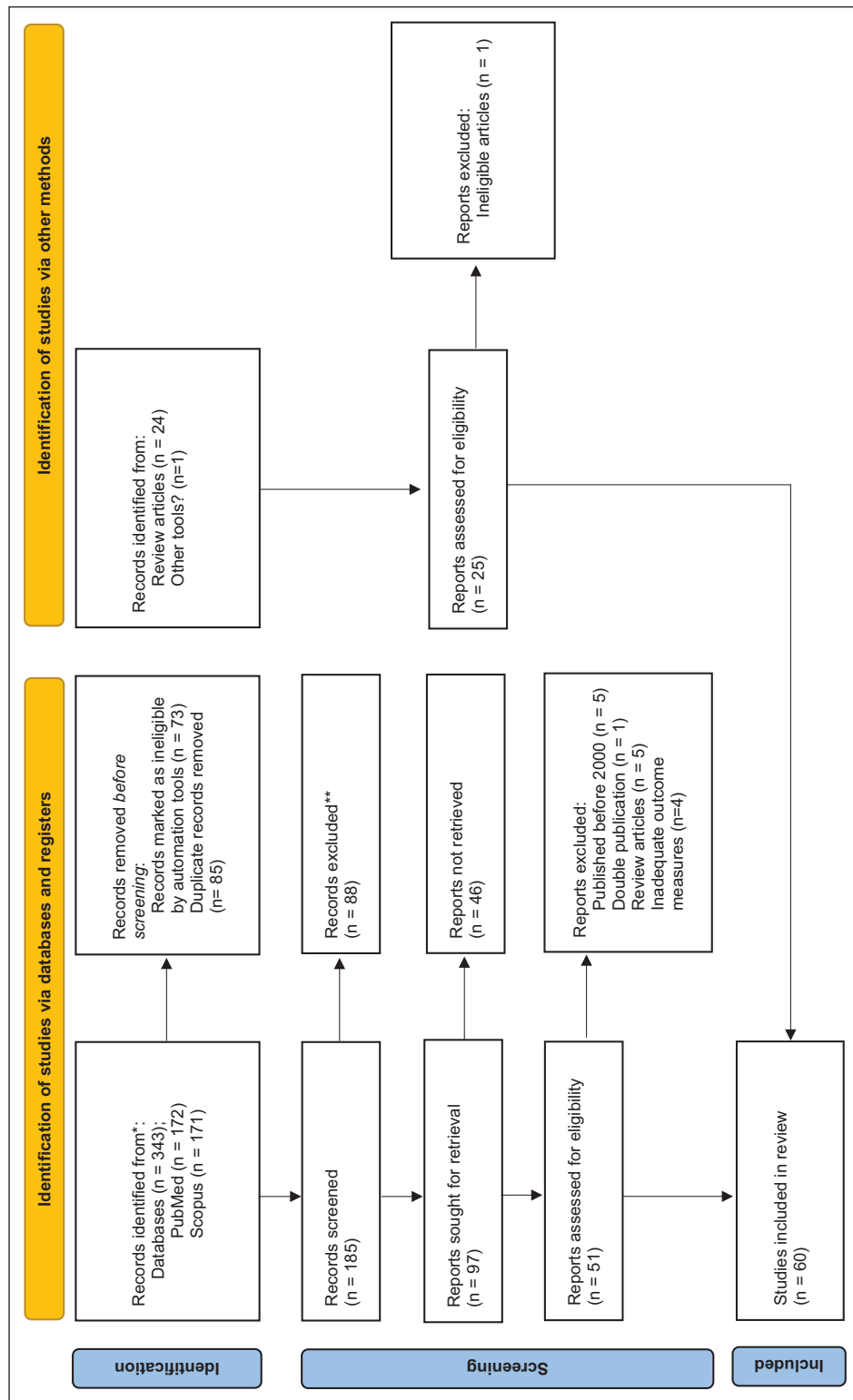


Fig. 1. PRISMA flow sheet describing the study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Eligibility criteria

Studies concerning non-obstetric surgery during pregnancy and its effects on the course of pregnancy with primary outcome measures of miscarriage, stillbirth, preterm birth, low birth weight, and an Apgar score less than 7 at 5 min were included in the review. The included studies were retrospective cohort studies, cross-sectional studies, and case series studies. We excluded studies published before 2000.

Data extraction and analysis

The extracted information is shown in Table 2 and includes author(s), year of publication, study design, participant information, study period, surgical intervention, outcome measures (miscarriage, stillbirth, preterm birth, low birth weight, Apgar score < 7, and infant and maternal morbidity and mortality), and the prevalence of non-obstetric surgery.

Odds ratios (ORs) with a 95% confidence interval (CI) were calculated to determine whether non-obstetric surgery was a risk for an adverse outcome of pregnancy and to estimate the magnitude of risk. Associations between categorical variables were tested using a chi-square test, and the Pearson correlation coefficient was calculated to measure the degree of association between the time of publication, sample size, and the proportion of laparoscopic procedures. A $p < 0.05$ was considered statistically significant.

Quality appraisal

A quality assessment was independently performed by two researchers (AH and HK). In case of disagreement, consensus was reached through dialogue. The quality of the reports was assessed according to the method described by Murad et al.⁹ in 2018, which included examining patient selection, adequate exposure and outcome ascertainment, causality, sufficient follow-up, adequate reporting, and hence the possibility of replicating the study.

Results

We gathered the data of 80,205 women who underwent non-obstetric surgery during pregnancy from 60 studies and of 16,655,486 women who had no surgery during pregnancy from 23 studies. The studies included are listed in Table 1.

Fourteen studies reported population-based data,^{10–12,15,22,23,26,29,31,33,35,42,45,50} three studies reported multicenter data^{36,39,60} and 43 studies reported single-center data,^{13,14,16–21,24,25,27,28,30,32,34,37,38,40,41,43,44,46–49,51–59,61–69} and all, except one small prospective single-center study on 22 women,⁶³ were retrospective.

The prevalence of non-obstetric surgery was between 0.31% and 0.73% (median 0.39%).^{11,12,22,23,25,29,35,60}

There was broad variation in the quality of the studies, since the selection method was unclear in many studies and some publications lacked precise outcome data and control group for the study population (Table 2).

Description of the studies according to the type of surgery

Appendectomy. Appendectomy is one of the most common surgeries during pregnancy, and 31 studies evaluated pregnancy outcomes in women who underwent this procedure.^{10,13,17,18,22,26,28,31,32,36–39,41,45,46,48–55,57,62–66,68,69}

There were data on 22,987 pregnant women who had an appendectomy during pregnancy. The median prevalence of appendectomies was 0.10%, but there was over a 10-fold difference, 0.03%–0.42%, between the studies ($n=15,430,217$). Based on data on 5754 women, 40% of appendectomies were performed in the first, 42% in the second, and 18% in the third trimester ($p < 0.001$, chi-square test). When the surgical approach was described ($n=14,373$), the laparoscopic technique was used in 39% of the procedures. Laparoscopy was used more commonly in the first (64% of cases) and the second trimester (47% of cases) but less frequently in the third trimester (16% of cases) ($p < 0.001$). The conversion rate in laparoscopic procedures ($n=332$) was 6%.

Cholecystectomy. Cholecystectomy is a common gastrointestinal surgery during pregnancy. Pregnancy outcomes were evaluated in four retrospective studies^{11,21,33,34} and in three laparoscopic feasibility studies.^{42,53,61} The median prevalence of cholecystectomy in 1891 women was 0.02% (range between 0.01% and 0.03%, $n=8,988,320$). There was one outlier; in the study by Buser,⁵⁶ the prevalence of cholecystectomy during pregnancy was 50 times higher at 0.97%. Based on data on 255 women, 41% of cholecystectomies were performed in the first, 49% in the second, and 10% in the third trimester ($p=0.005$). When the surgical approach was described ($n=83$), the laparoscopic technique was used in 89% of the procedures. Laparoscopy was used in the majority (86%–87%) of the cases in the first and the second trimesters, and in 60% of the cases in the third trimester ($p=0.142$). The conversion rate in the laparoscopic procedures ($n=59$) was relatively high, 14%.

Abdominal surgery in general. There were data for 8,934,684 pregnant women with 15,084 non-obstetric abdominal surgeries in general in 13 retrospective studies (prevalence 0.28%; range 0.19%–1.3%).^{11,16,23,24,27,30,35,40,47,53,56,58,65} The most common procedures were appendectomies, laparotomies, cholecystectomies, and anal and perianal surgeries. When it was described ($n=285$), 80% of procedures were emergent, and the laparoscopic technique was used in 66% of procedures. Based on data for 7020 women, 37% procedures were performed in

Table 1. The Quality assessment of the included studies according to Murad et al.⁹ Green color indicates sufficient quality and red color insufficient quality.

	Selection	Ascertainment 1	Ascertainment 2	Causality 1	Causality 2	Causality 3	Causality 4	Reporting
Haataja et al. ¹¹					NA	NA		
Fu et al. ¹²					NA	NA		
Chwat et al. ¹³					NA	NA		
Torres et al. ¹⁴					NA	NA		
Cho et al. ¹⁵					NA	NA		
Choi et al. ¹⁶					NA	NA		
Tanrıdan Okcu et al. ¹⁷					NA	NA		
Cho et al. ¹⁸					NA	NA		
Xiao et al. ¹⁹					NA	NA		
Moffatt et al. ²⁰					NA	NA		
Cho et al. ²¹					NA	NA		
Buitrago et al. ²²					NA	NA		
Rasmussen et al. ²³					NA	NA		
Vujic et al. ²⁴					NA	NA		
Devroe et al. ²⁵					NA	NA		
Ibibebe et al. ²⁶					NA	NA		
Cohen et al. ²⁷					NA	NA		
Gök et al. ²⁸					NA	NA		
Yu et al. ²⁹					NA	NA		
Kwon et al. ³⁰					NA	NA		
Won et al. ³¹					NA	NA		
Alkatary and Bahgat ³²					NA	NA		
Ibibebe et al. ³³					NA	NA		
Hedström et al. ³⁴					NA	NA		
Aylin et al. ³⁵					NA	NA		
Winter et al. ³⁶					NA	NA		
Segev et al. ³⁷					NA	NA		
Laustsen et al. ³⁸					NA	NA		
Yoo et al. ³⁹					NA	NA		
Shambe et al. ⁴⁰					NA	NA		
Karaman et al. ⁴¹					NA	NA		
Pamanathan et al. ⁴²					NA	NA		
Schwarzman et al. ⁴³					NA	NA		
Baldwin et al. ⁴⁴					NA	NA		
Cheng et al. ⁴⁵					NA	NA		
Peled et al. ⁴⁶					NA	NA		
Fardiazar et al. ⁴⁷					NA	NA		
Chung et al. ⁶⁹					NA	NA		
Jung et al. ⁴⁸					NA	NA		
Wei et al. ⁵⁰					NA	NA		
Hannan et al. ⁵¹					NA	NA		
Eom et al. ⁵²					NA	NA		
Choi et al. ⁴⁹					NA	NA		
Corneille et al. ⁵³					NA	NA		
Sadot et al. ⁵⁴					NA	NA		
Kirshtein et al. ⁵⁵					NA	NA		

(Continued)

Table I. (Continued)

	Selection	Ascertainment 1	Ascertainment 2	Causality 1	Causality 2	Causality 3	Causality 4	Reporting
Buser ⁵⁶					NA	NA		
McGory et al. ¹⁰					NA	NA		
Carver et al. ⁵⁷					NA	NA		
Rojansky et al. ⁵⁸					NA	NA		
Lee et al. ⁵⁹					NA	NA		
Jenkins et al. ⁶⁰					NA	NA		
Muench et al. ⁶¹					NA	NA		
Sakhri et al. ⁶²					NA	NA		
Lyass et al. ⁶³					NA	NA		
Hsu et al. ⁶⁴					NA	NA		
Gerstenfeld et al. ⁶⁵					NA	NA		
Mourad et al. ⁶⁶					NA	NA		
Usui et al. ⁶⁷					NA	NA		
Tracey and Fletcher ⁶⁸					NA	NA		

*Quality assessment: Selection: Does the patient(s) represent(s) the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?; Ascertainment 1: Was the exposure adequately ascertained?; Ascertainment 2: Was the outcome adequately ascertained?; Causality 1: Were other alternative causes that may explain the observation ruled out?; Causality 2: 5. Was there a challenge/rechallenge phenomenon?; Causality 3: Was there a dose–response effect?; Causality 4: Was follow-up long enough for outcomes to occur?; Reporting: Is the case(s) described with sufficient details?

the first, 40% in the second, and 23% in the third trimester ($p < 0.001$).

Non-obstetric gynecological surgery. Five studies evaluated pregnancy outcomes after non-obstetric gynecological surgery.^{11,15,21,59,67} There were data for 4,452,453 pregnant women with 4,281 non-obstetric gynecologic surgery (prevalence 0.08%). In a study by Cho et al.,¹⁵ laparoscopy was used in 44% of cases. In a study by Haataja et al.,¹¹ 32% of surgeries were performed in the first, 40% trimester, 40% in the second, and 28% in the third trimester ($p < 0.001$).

Trauma and orthopedic surgery. Ten studies reported data on trauma and orthopedic surgery.^{11,16,20,21,25,29,35,40,44,60} Based on data for 7,792,335 pregnant women, the prevalence of trauma surgery was 0.07%. Of note, the proportion of scheduled procedures was high; in the Haataja et al.¹¹ study 47% of the procedures were elective. Contrary to other types of surgeries that are commonly performed under general anesthesia, regional anesthesia was commonly used in trauma and orthopedic surgery cases. For example, in the Devroe et al.²⁵ study two-thirds of the cases were performed under regional anesthesia.

Non-obstetric surgery in general. Pregnancy outcomes after surgeries falling under different specialties were evaluated in 10 retrospective studies,^{11,12,16,21,25,29,35,43,44,60} There were data on 57,949 pregnancies where non-obstetric surgery was performed (prevalence 0.4%). Half of the procedures (52%) were scheduled, and half were emergency procedures (48%). In the first trimester, two-thirds (62%) of the procedures were scheduled, in the second

trimester 42%, and in the third trimester one third (33%) were scheduled procedures ($p < 0.001$). The most common types of surgical procedures were gastrointestinal (42%) and gynecological (20%), followed by trauma/orthopedic (12%), urological (7%), plastic surgery (4%), and neurosurgery (2%). The laparoscopic technique was used in 65% of intra-abdominal procedures, in 83% cases in the first, 38% in the second trimester, and 29% in the third trimester ($p < 0.001$).

Laparoscopic versus open surgery. We were also interested in studies comparing laparoscopic and open surgeries in abdominal cavity surgeries, and data were available from 32 studies for 36,120 pregnant women.^{10,17,21,22,24–26,28,30–32,34–39,41,45,46,48,49,52–55,57,58,63,65,68,69} In these studies, the use of these two approaches was similar; 47% of patients had laparoscopic and 53% open surgery. However, there was wide distribution between the studies, the lowest proportion of laparoscopic approach 5%²² and the highest 89%.³⁴ There was no correlation between the proportion of laparoscopy and time of the study ($r = -0.042$) or the sample size ($r = 0.092$), but between trimesters there was a significant difference; laparoscopy was used in 82% of procedures in the first, in 41% in the second, and in 27% of procedures in the third trimester ($p < 0.001$).

Comparison of trimesters

Data regarding the trimester when surgery was performed were available in the majority of the studies.^{11–14,16,17,19,21–25,28–30,32,35–39,41,42,47–51,53,54,56,59–63,66,68,69} There

Table 2. Description of included studies.

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Haataja et al. ¹¹	A retrospective, nationwide registry-based cohort study	Women with singleton pregnancies $n = 1,175,677$ Study period: 1997-2017	Non-obstetric surgery, $n = 4291$ (0.4%) First trimester $n = 1526$ (36%), second $n = 1524$ (36%), third $n = 1241$ (29%) Elective $n = 1465$ (66%), emergent $n = 2826$ (34%)	Fetal loss, PB, congenital anomalies, maternal mortality	OR with surgery vs no surgery: Fetal loss: $n = 15$ (0.3%) vs $n = 3619$ (0.3%), 1.1 [0.7-1.9] PB: $n = 394$ (9.2%) vs $n = 53,598$ (4.6%), 2.1 [1.9-2.3] Congenital anomalies: $n = 204$ (4.8%) vs $n = 48,550$ (4.1%), 1.2 [1.0-1.3] Maternal mortality: $n = 1$ vs $n = 39$, 7.0 [1.0-51.0] <ul style="list-style-type: none"> Gastrointestinal $n = 1904$ (44%) Gynecological $n = 692$ (16%) Orthopedic $n = 558$ (13%) Urologic $n = 351$ (8%) ENT surgery $n = 230$ (5%) Plastic surgery $n = 216$ (5%) Neurosurgery $n = 107$ (2%) Eye surgery $n = 93$ (2%) Endocrinological surgery $n = 52$ (1%) Vascular surgery $n = 30$ (> 1%) Thoracic surgery $n = 22$ (> 1%) Other $n = 37$ (> 1%)
Fu et al. ¹²	A retrospective, nationwide population-based case-control study	Women with singleton pregnancy, deliveries $n = 2,088,346$ Study period: 2004-2014	Non-obstetric surgery, $n = 4747$ (0.2%) Matched controls $n = 18,974$ First trimester $n = 2163$ (46%), second $n = 2059$ (43%), third $n = 525$ (11%)	Fetal loss, PB, LBW, Apgar score < 7, neonatal mortality	OR with surgery vs no surgery: Fetal loss: $n = 118$ (2.5%) vs $n = 241$ (1.3%), 2.0 [1.6-2.5] PB: $n = 632$ (13%) vs $n = 1540$ (8.1%), 1.7 [1.6-1.9] LBW: $n = 571$ (12%) vs $n = 1364$ (7.2%), 1.8 [1.6-2.0] Apgar score < 7: $n = 109$ (2.3%) vs $n = 256$ (1.4%); 1.7 [1.4-2.2] Neonatal mortality: $n = 26$ (0.6%) vs $n = 45$ (0.2%); 2.3 [1.4-3.8]
Chwat et al. ¹³	A single-center retrospective cohort study	Pregnant women with acute appendicitis, $n = 63$ Study period: 2005-2020	LS appendectomy, $n = 63$ (converted $n = 2$) First trimester $n = 16$ (25%), second $n = 38$ (60%), third $n = 9$ (14%)	MC, PB, SGA	MC: $n = 2$ PB: $n = 3$ SGA: $n = 1$ Postoperative complications: $n = 9$
Torres et al. ¹⁴	A single-center retrospective case series study	Pregnant women with non-obstetric surgery, $n = 6$ Study period: 2010-2019	Non-obstetric abdominal surgery, $n = 6$ First trimester $n = 2$, second $n = 4$	PB, LBW, Apgar score < 7, congenital anomalies	PB: $n = 1$ LBW: $n = 1$ Apgar score < 7: $n = 0$ Congenital anomalies: $n = 0$ <ul style="list-style-type: none"> LS appendectomy $n = 4$ Breast abscess $n = 1$ Ovarian torsion $n = 1$
Cho et al. ¹⁵	A retrospective, nationwide population-based cohort study	Pregnant women $n = 3,276,776$ Study period: 2006-2016	Non-obstetric abdominal surgery, $n = 8167$ (0.3%) LS $n = 3058$ (37%), open $n = 5109$ (63%)	PB, BW, LBW	OR with surgery vs no surgery: PB: $n = 372$ (5.2%) vs $n = 84,786$ (2.6%), 1.8 [1.6-2.0] BW: 3170 g vs 3220 g LBW: $n = 410$ (5.7%) vs $n = 115,377$ (3.5%), 1.4 [1.3-1.6] OR LS vs open surgery: PB: $n = 126$ (4.7%) vs $n = 246$ (5.4%), 0.8 [0.7-1.1] BW: 3180 g vs 3220 g LBW: $n = 149$ (5.6%) vs $n = 261$ (5.8%), 1.0 [0.8-1.2] <ul style="list-style-type: none"> Appendectomy $n = 4699$ (58%) Adnexal mass $n = 3468$ (42%)
Choi et al. ¹⁶	A single-center retrospective cohort study	Pregnant women with non-obstetric surgery, $n = 108$ Study period: 2009-2018	Non-obstetric surgery, $n = 108$ Elective $n = 9$ (8%), emergent $n = 97$ (92%) First trimester $n = 48$ (45%), second $n = 46$ (43%), third $n = 12$ (11%)	MC, fetal loss, PB, SGA, neonatal mortality, maternal mortality	MC: $n = 2$ Fetal loss: $n = 2$ PB: $n = 11$ SGA: $n = 4$ Neonatal mortality: $n = 1$ Maternal mortality: $n = 0$ OR LS ($n = 37$) vs open surgery ($n = 9$): PB: $n = 2$ (5.4%) vs $n = 1$ (11%), 0.5 [0.1-5.6] MC/fetal loss: $n = 3$ (8.1%) vs $n = 0$, 1.9 [0.1-40.7] SGA: $n = 2$ (5.4%) vs $n = 0$, 1.3 [0.1-30.3] <ul style="list-style-type: none"> Gastrointestinal $n = 42$ (40%) Orthopedic $n = 25$ (24%) Genito-urinary $n = 17$ (16%) Other $n = 22$ (21%)

(Continued)

Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Tanrıdan Okcu et al. ¹⁷	A single-center retrospective case series study	Pregnant <i>n</i> = 48,120 Study period: 2011-2017	Non-obstetric abdominal surgery, <i>n</i> = 75 (0.16%) Appendectomy, <i>n</i> = 50 (0.1%); LS <i>n</i> = 6 (12%), open <i>n</i> = 44 (88%) First trimester <i>n</i> = 8 (16%), second <i>n</i> = 25 (50%), third <i>n</i> = 17 (34%)	MC, PB, Apgar score \leq 5, congenital anomalies, neonatal mortality, maternal mortality, complications	Appendectomy, <i>n</i> = 50 MC: <i>n</i> = 1 PB: 4 Apgar score \leq 5: <i>n</i> = 2 Congenital anomalies: <i>n</i> = 1 Neonatal mortality: <i>n</i> = 2 Maternal mortality: <i>n</i> = 0 Wound infection: <i>n</i> = 2 • Gastrointestinal <i>n</i> = 57 • Gynecological <i>n</i> = 6 • NA <i>n</i> = 12
Cho et al. ¹⁸	A single-center retrospective cohort study	Pregnant women with acute appendicitis, <i>n</i> = 12 Study period: 2014-2016	LS appendectomy, <i>n</i> = 12 (converted <i>n</i> = 0)	MC, congenital anomalies, complications	MC: <i>n</i> = 1 Congenital anomalies: <i>n</i> = 1 Wound infection: <i>n</i> = 2 Post-operative ileus: <i>n</i> = 1
Xiao et al. ¹⁹	A single-center retrospective case series study	Pregnant women who underwent LS gynecological surgery, <i>n</i> = 13 Study period: 2015-2019	Non-obstetric LS gynecological surgery, <i>n</i> = 11 (converted <i>n</i> = 0) First trimester <i>n</i> = 6, second <i>n</i> = 5	PB, LBW, Apgar score < 7	PB: <i>n</i> = 2 LBW: <i>n</i> = 1 Apgar score < 7: <i>n</i> = 0
Moffatt et al. ²⁰	A single-center retrospective cohort study	Pregnant women having trauma injuries, <i>n</i> = 89 Study period: 2012-2018	Non-obstetric trauma surgery, <i>n</i> = 46	Fetal loss, PB, maternal mortality	Fetal loss: <i>n</i> = 16 PB: <i>n</i> = 0 Maternal mortality: <i>n</i> = 3 • Laparotomy <i>n</i> = 140.5 [0.5 • Wound debridement <i>n</i> = 11 • Orthopedic <i>n</i> = 8 • Other <i>n</i> = 13
Cho et al. ²¹	A single-center retrospective cohort study	Pregnant women, <i>n</i> = 16,197 Study period: 2001-2016	Non-obstetric surgery, <i>n</i> = 155 (1.0%) Open <i>n</i> = 104, LS <i>n</i> = 51 First trimester <i>n</i> = 77 (50%), second <i>n</i> = 62 (40%), third <i>n</i> = 16 (10%) Elective <i>n</i> = 49 (32%), emergent <i>n</i> = 106 (68%)	MC, fetal loss, PB, BW, maternal mortality	MC: <i>n</i> = 6 Fetal loss: <i>n</i> = 7 PB: <i>n</i> = 7 Maternal mortality <i>n</i> = 1 OR LS (<i>n</i> = 18) vs open surgery (<i>n</i> = 27) Fetal loss: <i>n</i> = 4 (22.2%) vs <i>n</i> = 1 (3.7%), 7.4 [0.8-73.0] PB: <i>n</i> = 1 (5.6%) vs <i>n</i> = 3 (11.1%), 0.5 [0.1-4.9] BW: 3100 g vs 3200 g • Appendectomy <i>n</i> = 61 (39%) • Cholecystectomy <i>n</i> = 7 (5%) • Gynecological <i>n</i> = 56 (36%) • Orthopedic <i>n</i> = 10 (7%) • Breast surgery <i>n</i> = 8 (5%) • Other <i>n</i> = 13 (8%)
Buitrago et al. ²²	A retrospective, nationwide registry-based cohort study	Pregnant women, deliveries, <i>n</i> = 1,529,807 Study period: 2011-2016	Appendectomy <i>n</i> = 2507 (0.2%) First trimester <i>n</i> = 885 (35%), second <i>n</i> = 1205 (48%), third <i>n</i> = 417 (17%) LS <i>n</i> = 113 (5%) Open <i>n</i> = 2394 (95%)	PB, birth \leq 32 GW, BW, BW < 1750 g, Apgar score < 7	OR third vs first/second trimester: PB: 2.0 [1.5-2.7] \leq 32 GW: 2.5 [1.5-4.1] BW: 2966 g vs 3065 g BW < 1750 g: 2.7 [1.6-4.4] Apgar score < 7: 2.5 [0.9-7.4]
Rasmussen et al. ²³	A retrospective, nationwide registry-based cohort study	Women with singleton birth or MC; <i>n</i> = 1,202,870 Study period: 1997-2015	Non-obstetric abdominal surgery, <i>n</i> = 4490 (0.4%) First trimester <i>n</i> = 1693 (38%), second <i>n</i> = 1748 (39%), third <i>n</i> = 1049 (23%)	MC, birth < 32 GW, PB, SGA	OR with surgery vs no surgery: MC: <i>n</i> = 241 (8.2%) vs <i>n</i> = 72,521 (6.1%); 1.4 [1.2-1.6] birth < 32 GW: <i>n</i> = 78 (2.2%) vs <i>n</i> = 8709 (0.8%); 2.9 [2.3-3.7] PB: <i>n</i> = 424 (10%) vs <i>n</i> = 55,811 (5.0%); 2.1 [1.9-2.4] SGA: 128 (3.4%) vs 30,392 (2.7%); 1.2 [1.0-1.4] • Appendectomy 30% • Laparotomy 27% • Anal and perianal surgery 13% • Cholecystectomy 9% • Hemorrhoids 7%

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Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Vujic et al. ²⁴	A single-center retrospective cohort study	Pregnant women Study period: 2005-2015	Non-obstetric abdominal surgery <i>n</i> = 76 First trimester <i>n</i> = 15, second <i>n</i> = 44, third <i>n</i> = 17 Elective <i>n</i> = 14, emergent <i>n</i> = 62. LS <i>n</i> = 19, open <i>n</i> = 57	MC, PB, neonatal morbidity and mortality, maternal morbidity and mortality	MC: <i>n</i> = 5 PB: <i>n</i> = 12 Neonatal morbidity: <i>n</i> = 9 Maternal morbidity: <i>n</i> = 4 Neonatal or maternal mortality: no <ul style="list-style-type: none"> • Appendectomy: LS <i>n</i> = 6, open <i>n</i> = 42 • Cholecystectomy <i>n</i> = 4 • Gynecological <i>n</i> = 8 • Other <i>n</i> = 16
Devroe et al. ²⁵	A single-center retrospective matched case-control cohort study	Delivered women <i>n</i> = 35,612 Study period: 2001-2016	Non-obstetric surgery; patients <i>n</i> = 171 (0.5%), procedures <i>n</i> = 189 First trimester <i>n</i> = 54, second <i>n</i> = 75, third <i>n</i> = 42 Matched controls <i>n</i> = 684	Fetal loss, PB, BW, LBW < 2 500g	OR with surgery vs matched controls: Fetal loss: <i>n</i> = 3 (1.8%) vs <i>n</i> = 535 (1.5%); 1.2 [0.4-3.7] PB: <i>n</i> = 44 (25%) vs <i>n</i> = 114 (17%); 1.7 [1.2-2.6] BW: 3160g vs 3270g LBW: <i>n</i> = 32 (18%) vs 95 (14%); 1.4 [0.9-2.2] <ul style="list-style-type: none"> • Gastrointestinal: LS <i>n</i> = 55, open <i>n</i> = 27 • Gynecological: LS <i>n</i> = 11, open <i>n</i> = 11 • Orthopedic: <i>n</i> = 29 • Urology: <i>n</i> = 16 • Oncological: <i>n</i> = 15 • Others <i>n</i> = 25
Ibibebe et al. ²⁶	A retrospective, nationwide population-based cohort study	Women with singleton pregnancy ≥ 20 GW <i>n</i> = 1,124,551 Study period: 2002-2014	Appendectomy <i>n</i> = 1024 (0.1%) LS <i>n</i> = 566 Open <i>n</i> = 458	Fetal loss, PB, SGA, Apgar score < 7, neonatal morbidity, neonatal mortality, maternal morbidity	OR with surgery vs no surgery: Fetal loss: <i>n</i> = 4 (0.4%) vs <i>n</i> = 6481 (0.6%), OR 0.7 [0.3-1.9] PB: <i>n</i> = 105 (10.6%) vs <i>n</i> = 66,687 (5.9%), OR 1.9 [1.5-2.3] SGA: <i>n</i> = 87 (8.5%) vs 108294 (9.6%), OR 0.9 [0.7-1.1] Apgar score < 7: <i>n</i> = 24 (2.4%) vs <i>n</i> = 22,403 (2.0%), OR 1.2 [0.8-1.8] Neonatal morbidity: <i>n</i> = 62 (6.1%) vs <i>n</i> = 46063 (4.1%), OR 1.5 [1.2-1.9] Neonatal mortality: <i>n</i> = 4 (0.4%) vs <i>n</i> = 2165 (0.2%), OR 2.1 [0.8-5.6] Maternal morbidity: <i>n</i> = 50 (4.9%) vs <i>n</i> = 19864 (1.8%), OR 2.9 [2.1-3.8]
Cohen et al. ²⁷	A single-center retrospective case series study	Pregnant women ≥ 27 GW with LS surgery. Study period: 2010-2017	Non-obstetric emergent LS surgery <i>n</i> = 12 (converted <i>n</i> = 1)	PB, BW, SGA, Apgar score < 7, maternal morbidity	PB: <i>n</i> = 2 BW: 3005g SGA: <i>n</i> = 1 Apgar score < 7: <i>n</i> = 1 Surgical site infection: <i>n</i> = 1 Premature contractions: <i>n</i> = 1 <ul style="list-style-type: none"> • Appendectomy: <i>n</i> = 7 • Adnexal torsion release: <i>n</i> = 4 • Diagnostic LS: <i>n</i> = 1
Gök et al. ²⁸	A single-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 57 Study period 2009-2018	Appendectomy <i>n</i> = 57 LS <i>n</i> = 18 (first trimester <i>n</i> = 7, second <i>n</i> = 10, third <i>n</i> = 1) Open <i>n</i> = 39 (first <i>n</i> = 11, second <i>n</i> = 19, third <i>n</i> = 9).	Fetal loss, PB, maternal morbidity	LS vs open surgery: Fetal loss: <i>n</i> = 0 vs <i>n</i> = 1 PB: <i>n</i> = 0 vs <i>n</i> = 2 Surgical site infection: <i>n</i> = 1 vs <i>n</i> = 3
Yu et al. ²⁹	A retrospective, nationwide population-based case-control study	Pregnant women <i>n</i> = 118,851 Study period: 1997-2013	Non-obstetric surgery <i>n</i> = 462 (0.4%) first trimester = 167 (36%), second <i>n</i> = 232 (50%), third <i>n</i> = 63 (14%). Elective <i>n</i> = 352 (76%), emergent <i>n</i> = 110 (24%);	MC, PB, maternal mortality	OR with surgery vs no surgery: MC: <i>n</i> = 22 (4.8%) vs <i>n</i> = 3997 (3.4%), 1.4 [0.9-2.2] PB: <i>n</i> = 36 (7.8%) vs <i>n</i> = 5064 (4.3%), 1.9 [1.3-2.7] Maternal mortality: <i>n</i> = 1 vs <i>n</i> = 72, 3.6 [0.5-25.72] <ul style="list-style-type: none"> • Gynecological: <i>n</i> = 258 • Gastrointestinal: <i>n</i> = 115 • Musculoskeletal: <i>n</i> = 40 • Other: <i>n</i> = 49
Kwon et al. ³⁰	A single-center retrospective cohort study	Pregnant women with non- obstetric surgery <i>n</i> = 62 Study period: 2008-2016	Non-obstetric surgery <i>n</i> = 62 LS <i>n</i> = 35 (first trimester <i>n</i> = 15, second <i>n</i> = 15, third <i>n</i> = 5) Open <i>n</i> = 27 (first <i>n</i> = 7, second <i>n</i> = 17, third <i>n</i> = 3)	PB, maternal morbidity	OR LS vs open surgery: PB: <i>n</i> = 2 vs <i>n</i> = 4, 0.3 [0.1-2.1] Wound infection: <i>n</i> = 1 vs <i>n</i> = 3, 0.2 [0.1-2.4] <ul style="list-style-type: none"> • Appendectomy: open <i>n</i> = 21, LS <i>n</i> = 18 • Cholecystectomy: open <i>n</i> = 2, LS <i>n</i> = 2 • Gynecological: open <i>n</i> = 4, LS <i>n</i> = 15

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Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Won et al. ³¹	A retrospective, nationwide population-based cohort study	Women aged 15-45 years with appendectomy, <i>n</i> = 62,118 Study period: 2005-2011	Pregnant women with appendectomy <i>n</i> = 4047 (LS 55%)	Fetal loss, PB, maternal morbidity	OR appendectomy vs no appendectomy: Fetal loss: 1.1% vs 1.1%, 1.0 [0.9-1.2] PB: 9.1% vs 8.9%, 1.0 [0.9-1.1] Maternal morbidity: 3.4% vs 2.7%, 1.3 [1.1-1.5]
Alkatary and Bahgat ³²	A single-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 23 Study period 2010-2012	Appendectomy <i>n</i> = 21 LS <i>n</i> = 9 (first trimester <i>n</i> = 3, second <i>n</i> = 4, third <i>n</i> = 2) Open <i>n</i> = 12 (first <i>n</i> = 3, second <i>n</i> = 3, third <i>n</i> = 6)	Fetal loss, PB, congenital anomalies, maternal morbidity	OR LS vs open surgery: Fetal loss: no PB: <i>n</i> = 1 vs <i>n</i> = 1, 1.4 [0.1-25.4] Congenital anomalies: no Postoperative wound infection: 0 vs. 2, 0.2 [0.1-5.2]
Ibibebe et al. ³³	A retrospective, nationwide population-based cohort study	Women with singleton pregnancies <i>n</i> = 1,064,089 Study period: 2001-2012	Gallstone disease <i>n</i> = 1882 Cholecystectomy <i>n</i> = 239 (0.02%)	PB, Apgar score < 7, SGA, neonatal morbidity, maternal morbidity	OR cholecystectomy vs conservative management vs no gallstone disease: PB: <i>n</i> = 18 (7.5%) vs <i>n</i> = 137 (8.3%), 0.9 [0.5-1.5], vs <i>n</i> = 62,606 (5.9%), 1.3 [0.8-2.1] Apgar score < 7: <i>n</i> = 10 (4.2%) vs <i>n</i> = 29 (1.8%), 2.4 [1.2-5.1] vs <i>n</i> = 20,934 (2.0%), 2.1 [1.6-4.1] SGA: 24 (10%) vs 168 (8.9%), 1.0 [0.6-1.5] vs <i>n</i> = 104,325 (9.9%), 1.0 [0.7-1.6] Neonatal morbidity: <i>n</i> = 14 (5.9%) vs <i>n</i> = 105 (6.4%), 0.9 [0.5-1.6] vs 44,988 (4.2%), 1.4 [0.8-2.4] Maternal morbidity: <i>n</i> = 8 (3.4%) vs <i>n</i> = 47 (2.9%), 1.2 [0.5-2.5] vs 18,305 (1.7%), 2.0 [1.0-4.0]
Hedström et al. ³⁴	A single-center retrospective cohort study	Pregnant women <i>n</i> = 119,189. Study period: 2001-2015	Pregnant women with gallstone disease in pregnancy <i>n</i> = 97 (0.03%) Surgery <i>n</i> = 35 (LS <i>n</i> = 31, open <i>n</i> = 4) Conservative <i>n</i> = 62	MC, PB, LBW < 2500g, BW	OR surgery vs conservative treatment: MC: <i>n</i> = 1 vs <i>n</i> = 2, 0.9 [0.1-10.1] PB: <i>n</i> = 2 vs <i>n</i> = 13, 0.2 [0.1-1.1] LBW: <i>n</i> = 1 vs <i>n</i> = 4, 0.4 [0.1-4.0] BW: 3358g vs 3512g
Aylin et al. ³⁵	A retrospective, nationwide population-based cohort study	Pregnant women, <i>n</i> = 6,486,280 Study period: 2002-2011	Non-obstetric surgery, <i>n</i> = 47,628 (0.7%) First trimester 45%, second 26%, third 29% Elective (53%) Emergent (47%)	MC, fetal loss, PB, LBW, maternal mortality	OR with surgery vs no surgery: MC: <i>n</i> = 3120 (6.6%) vs <i>n</i> = 373,203 (5.8%), 1.1 [1.1-1.2] Fetal loss: <i>n</i> = 411 (0.9%) vs <i>n</i> = 33,363 (0.5%), 1.7 [1.5-1.8] PB: <i>n</i> = 4916 (10.7%) vs <i>n</i> = 452,877 (7.2%), 1.5 [1.5-1.6] LBW: <i>n</i> = 3831 (11.1%) vs <i>n</i> = 338,800 (7.0%), 1.6 [1.6-1.7] Maternal mortality: <i>n</i> = 12 (0.03%) vs <i>n</i> = 223 (<0.01%), 7.3 [4.1-13.0] • Abdominal: <i>n</i> = 12,493 (26%) • Dental: <i>n</i> = 5365 (11%) • Nail and skin: <i>n</i> = 4762 (10%) • Orthopedic: <i>n</i> = 4563 (9.6%) • Ear, nose, throat: <i>n</i> = 3060 (6.4%) • Perianal: <i>n</i> = 2977 (6.2%) • Breast surgery: <i>n</i> = 1884 (<i>n</i> = 4.0%) • Other: <i>n</i> = 12,524 (26%)
Winter et al. ³⁶	A seven-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 218 Study period 2000-2012	Appendectomy <i>n</i> = 218 LS <i>n</i> = 125 (converted <i>n</i> = 5) (first trimester <i>n</i> = 67, second <i>n</i> = 54, third <i>n</i> = 4) Open <i>n</i> = 93 (first <i>n</i> = 13, second <i>n</i> = 58, third <i>n</i> = 22)	MC, fetal loss, PB	OR LS vs open surgery: MC: <i>n</i> = 6 (4.8%) vs <i>n</i> = 0, 10.2 [0.6-182.9] Fetal loss: <i>n</i> = 1 (0.8%) vs <i>n</i> = 0, 2.3 [0.1-55.9] PB: <i>n</i> = 8 (6.8%) vs <i>n</i> = 8 (8.6%), 0.8 [0.3-2.2]
Segev et al. ³⁷	A single-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 92 Study period: 2000-2014	Appendectomy <i>n</i> = 92 LS <i>n</i> = 50 (converted <i>n</i> = 2) (first trimester <i>n</i> = 20, second <i>n</i> = 29, third <i>n</i> = 1) Open <i>n</i> = 42 (first <i>n</i> = 6, second <i>n</i> = 16, third <i>n</i> = 20)	MC, PB, BW, Apgar score < 7, maternal morbidity	OR LS vs open surgery: MC: <i>n</i> = 2 (8%) vs <i>n</i> = 2 (5%), 2.1 [0.3-15.8] PB: <i>n</i> = 5 (20%) vs <i>n</i> = 3 (9%), 2.5 [0.5-11.7] BW: 3000g vs 3400g Apgar score < 7: none Premature contractions: <i>n</i> = 4 (9%) vs <i>n</i> = 5 (12%), 0.7 [0.2-3.0] Wound infection: <i>n</i> = 0 vs <i>n</i> = 5 (12%), 0.1 [0.0-2.5]

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Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Laustsen et al. ³⁸	A single-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 44 Study period 2000-2011	Appendectomy <i>n</i> = 44 LS <i>n</i> = 19 (converted <i>n</i> = 2) (first trimester <i>n</i> = 8, second <i>n</i> = 7, third <i>n</i> = 4) Open <i>n</i> = 25 (second <i>n</i> = 20, third <i>n</i> = 5)	Fetal loss, PB, BW, neonatal mortality, maternal morbidity	OR LS vs open surgery: Fetal loss: no PB: <i>n</i> = 3 vs <i>n</i> = 2, 2.2 [0.3-14.4] BW: 3458 g vs 3366 g Neonatal mortality: no Wound infection/abscess: <i>n</i> = 1 vs <i>n</i> = 8, 0.1 [0.1-1.0]
Yoo et al. ³⁹	A six-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> = 80 Study period 2008-2015	Appendectomy <i>n</i> = 80 LS <i>n</i> = 24 (first trimester <i>n</i> = 7, second <i>n</i> = 15, third <i>n</i> = 2; no conversion) Open <i>n</i> = 56 (first <i>n</i> = 14, second <i>n</i> = 29, third <i>n</i> = 13)	Fetal loss, PB, BW, maternal morbidity	OR LS vs open surgery: Fetal loss: <i>n</i> = 3 vs <i>n</i> = 4, 1.9 [0.4-9.0] PB: <i>n</i> = 2 vs <i>n</i> = 4, 1.2 [0.2-6.9] BW: 2860 g vs 2840 g Wound infection/abscess: <i>n</i> = 4 vs <i>n</i> = 6, 1.7 [0.4-6.5]
Shambe et al. ⁴⁰	A single-center retrospective cross-sectional study	Pregnant women with births <i>n</i> = 10,769 Study period: 2007-2011	Emergent non-obstetric abdominal surgery, <i>n</i> = 50 (0.5%) second trimester <i>n</i> = 33	MC, fetal loss, maternal mortality	MC: <i>n</i> = 11 Fetal loss: <i>n</i> = 1 Maternal mortality: <i>n</i> = 1 • Appendectomy <i>n</i> = 43 • Gunshot injury <i>n</i> = 6 • Other <i>n</i> = 1
Karaman et al. ⁴¹	A single-center retrospective cohort study	Pregnant women Study period: 2010-2015	Appendectomy <i>n</i> = 48 LS <i>n</i> = 12 (first trimester <i>n</i> = 1, second <i>n</i> = 7, third <i>n</i> = 4) Open <i>n</i> = 36 (first <i>n</i> = 2, second <i>n</i> = 12, third <i>n</i> = 22)	MC, fetal loss, PB, maternal morbidity	OR LS vs open surgery: MC: <i>n</i> = 1 vs <i>n</i> = 0, 9.5 [0.3-250.2] Fetal loss: <i>n</i> = 0 vs <i>n</i> = 1, 0.9 [0.1-24.8] PB: <i>n</i> = 3 vs <i>n</i> = 9, 1.0 [0.2-4.5] Wound infection: <i>n</i> = 1 vs <i>n</i> = 1, 3.2 [0.2-55.2]
Paramanathan et al. ⁴²	A retrospective, nationwide population-based cohort study	Pregnant women with LS cholecystectomy <i>n</i> = 22 Study period: 2003-2013	LS cholecystectomy <i>n</i> = 22 (converted <i>n</i> = 3) First trimester <i>n</i> = 2, second <i>n</i> = 18, third <i>n</i> = 2	Fetal loss, PB, BW, maternal morbidity	Fetal loss: no PB: <i>n</i> = 2 BW: 3220 g Maternal morbidity: <i>n</i> = 4
Schwarzman et al. ⁴³	A single-center retrospective comparative cohort study	Pregnant women Study period: 1992-2012	Non-obstetric surgery <i>n</i> = 61 Matched controls <i>n</i> = 122	PB, BW, Apgar score < 7	OR surgery vs control deliveries: PB: <i>n</i> = 11 (18%) vs <i>n</i> = 5 (10%), 2.0 [0.7-6.3] BW: 2910 g vs 3190 g Apgar score < 7: <i>n</i> = 0 vs 0 • Appendectomy <i>n</i> = 13 • Intra-abdominal abscess drainage <i>n</i> = 9 • Other abdominal surgery <i>n</i> = 9 • Urologic <i>n</i> = 9 • Gynecologic <i>n</i> = 8 • Other <i>n</i> = 13
Baldwin et al. ⁴⁴	A single-center retrospective cohort study	Pregnant women ≥ 23 GW, <i>n</i> = 36,100 Study period: 1992-2014	Surgical procedures <i>n</i> = 121 in <i>n</i> = 111 women (0.3%)	Fetal loss, PB	Fetal loss <i>n</i> = 1 PB: <i>n</i> = 35 (41%) • Abdominal surgery <i>n</i> = 42 • Renal <i>n</i> = 17 • Orthopedic <i>n</i> = 7 • Gynecologic <i>n</i> = 4 • Neurosurgery: <i>n</i> = 4 • Other <i>n</i> = 12
Cheng et al. ⁴⁵	A nationwide retrospective population-based study	Pregnant women <i>n</i> = 1,147,214 Study period 2005-2010	Appendicitis 859 (0.07%); Appendectomy <i>n</i> = 781 LS <i>n</i> = 128 Open <i>n</i> = 653; Antibiotic only <i>n</i> = 78; Control group <i>n</i> = 3436	Fetal loss, PB	OR: antibiotic / LS / open surgery vs control: Fetal loss: 12% / 5.5% / 5.7% / 0.4%; OR 31.9 [13.3-76.1] / 14.1 [5.6-35.7] / 14.7 [7.9-27.3] PB: 10.3% / 5.5% / 11.3% vs 4.4%; OR 2.5 [1.2-5.3] / 1.3 [0.6-2.7] / 2.8 [2.1-3.7]
Peled et al. ⁴⁶	A single-center retrospective cohort study	Pregnant women <i>n</i> = 83,510 Study period: 2000-2009	Appendectomy <i>n</i> = 85 (0.1%); LS <i>n</i> = 26 (no conversions) Open <i>n</i> = 59	MC, PB, BW, maternal morbidity	OR LS vs open surgery: MC: <i>n</i> = 1 vs <i>n</i> = 0, 7.0 [0.3-177.7] PB: <i>n</i> = 5 vs <i>n</i> = 14, 0.8 [0.2-2.4] BW: 3075 g vs 3115 g Postoperative fever/premature contractions: 1 vs 15, 0.1 [0.1-0.9]

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Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Fardiazar et al. ⁴⁷	A single-center retrospective cross-sectional study	Pregnant women with non-obstetric abdominal surgery $n = 100$ Study period: 2007-2012	Non-obstetric abdominal surgery $n = 100$ first trimester $n = 28$, second $n = 48$, third $n = 24$	Fetal loss, fetal distress, asphyxia	Fetal loss: $n = 2$ Fetal distress: $n = 4$ Asphyxia: $n = 5$ <ul style="list-style-type: none"> • Appendectomy $n = 61$ • Cholecystectomy $n = 6$ • Other abdominal $n = 4$ • Gynecologic $n = 30$
Chung et al. ⁶⁹	A single-center prospective cohort study	Pregnant women with appendectomy $n = 61$ Study period: 2007-2011	Appendectomy $n = 61$: LS $n = 22$ (first trimester $n = 6$, second $n = 13$, third $n = 3$) Open $n = 39$ (first $n = 8$, second $n = 20$, third $n = 11$)	Fetal loss, PB, BW, maternal morbidity	OR LS vs open surgery: Fetal loss: no PB: $n = 2$ vs $n = 4$, 0.9 [0.1-5.2] BW: 2810 g vs 2790 g Abscess/wound infection: $n = 1$ vs $n = 2$, 0.9 [0.1-10.6]
Jung et al. ⁴⁸	A single-center retrospective cross-sectional study	Pregnant women $n = 14,203$ Study period: 2004-2010	Appendectomy $n = 25$ (0.2%): LS $n = 4$ (first trimester $n = 3$, second $n = 1$) Open $n = 21$ (first $n = 7$, second $n = 13$, third $n = 1$)	MC, PB, maternal mortality, maternal morbidity	MC: $n = 2$ PB: no Maternal mortality: no OR LS vs open surgery: Wound infection: 0 vs 2, 0.9 [0.1-21.4]
Wei et al. ⁵⁰	A retrospective, nationwide population-based cross-sectional study	Women with live singleton births $n = 218,776$ Study period: 2005	Appendectomy $n = 908$ (0.4%) First trimester $n = 780$, second $n = 85$, third $n = 43$ Matched controls $n = 4540$	PB, LBW, SGA, Apgar score < 7, congenital anomalies	OR appendectomy vs controls: PB: $n = 105$ (12%) vs 329 (7.3%), 1.6 [1.3-2.0] LBW: 109 (12%) vs 309 (6.8%), 1.8 [1.4-2.3] SGA: 203 (22%) vs 796 (18%), 1.3 [1.1-1.6] Apgar score < 7: $n = 5$ (0.4%) vs $n = 9$ (0.2%), 2.5 [0.7-8.8] Congenital anomalies: $n = 13$ (1.4%) vs $n = 30$ (0.7%), 2.1 [1.1-4.0]
Hannan et al. ⁵¹	A single-center retrospective cross-sectional study	Pregnant women with LS appendectomy $n = 31$ Study period: 2005-2010	LS appendectomy $n = 31$ First trimester $n = 9$, second $n = 18$, third $n = 4$	MC, PB, congenital anomalies	MC $n = 1$ PB: $n = 1$ Congenital anomalies: $n = 1$
Eom et al. ⁵²	A single-center retrospective cohort study	Pregnant women with right lower quadrant pain $n = 76$ Study period: 2000-2010	Appendectomy $n = 43$ LS $n = 15$ Open $n = 28$ No intervention $n = 33$	MC/fetal loss, PB, BW, Apgar score < 7, maternal morbidity	OR LS vs open surgery: MC/fetal loss: 1 vs 2, 1.1 [0.1-13.2] PB: $n = 0$ vs $n = 3$, 0.3 [0.1-5.7] BW: 3125 g vs 2780 g Apgar score < 7: NA vs $n \geq 1$ Premature contractions: $n = 1$ vs $n = 3$, 0.7 [0.1-7.5] Intraperitoneal abscess: $n = 0$ vs $n = 1$, 0.7 [0.1-18.2] Postoperative fever: $n = 0$ vs $n = 3$, 0.3 [0.1-5.7]
Choi et al. ⁴⁹	A single-center retrospective cross-sectional study	Pregnant women with appendectomy $n = 52$ Study period: 2000-2009	Appendectomy $n = 52$ LS $n = 24$ (converted $n = 2$) (first trimester $n = 7$, second $n = 12$, third $n = 5$) Open $n = 5$ (second $n = 2$, third $n = 3$)	Fetal loss, BW, neonatal mortality, developmental delays, maternal morbidity	Fetal loss: $n = 1$ BW: 3361 g Neonatal mortality: no Developmental delays: no Maternal morbidity: $n = 1$ (fever)
Cornelle et al. ⁵³	A single-center retrospective cohort study	Pregnant women non-obstetric abdominal surgery $n = 94$ Study period: 1993-2007	Non-obstetric abdominal surgery $n = 94$ LS $n = 53$ (converted $n = 2$) (first trimester $n = 21$, second $n = 28$, third $n = 4$) Open $n = 41$ (first $n = 19$, second $n = 12$, third $n = 10$)	MC, fetal loss, PB, SGA	OR LS vs open surgery: MC: $n = 1$ vs $n = 2$, 0.4 [0.1-4.3] Fetal loss: $n = 0$ vs $n = 1$, 0.2 [0.1-6.4] PB: $n = 4$ vs $n = 5$, 0.6 [0.1-2.3] SGA: $n = 1$ vs $n = 0$, 2.4 [0.1-59.7] <ul style="list-style-type: none"> • Appendectomy: LS $n = 9$ (conversion 1), open $n = 40$ • Cholecystectomy: LS $n = 39$ (conversion 1), open $n = 1$ • Salpingectomy/cystectomy: LS $n = 5$

(Continued)

Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Sadot et al. ⁵⁴	A single-center retrospective cohort study	Pregnant women with appendectomy <i>n</i> =65 Study period: 1999-2008	Appendectomy <i>n</i> =65 LS <i>n</i> =48 (first trimester <i>n</i> =14, second <i>n</i> =32, third <i>n</i> =2) Open <i>n</i> =17 (second <i>n</i> =12, third <i>n</i> =5)	Fetal loss, PB, BW, maternal morbidity	OR LS vs open surgery: Fetal loss: <i>n</i> =1 vs <i>n</i> =0, 1.2 [0.1-31.6] PB: 12 (29%) vs 3 (19%), 1.8 [0.4-7.5] BW: 3297 g vs 3311 g Wound infection/abscess: <i>n</i> =1 vs <i>n</i> =1, 0.3 [0.1-5.8] Hemoperitoneum: <i>n</i> =1 vs <i>n</i> =0, 1.1 [0.1-28.4] Premature contractions: <i>n</i> =1 vs <i>n</i> =1, 0.3 [0.1-5.8]
Kirshstein et al. ⁵⁵	A single-center retrospective cohort study	Pregnant women with appendectomy during first and second trimester <i>n</i> =42 Study period: 1997-2007	Appendectomy <i>n</i> =42 First trimester <i>n</i> =23, second <i>n</i> =19) LS <i>n</i> =23 (converted <i>n</i> =1) Open <i>n</i> =19	MC, BW, premature contractions, maternal morbidity	OR LS vs open surgery: MC: <i>n</i> =1 vs <i>n</i> =1, 0.8 [0.1-14.0] BW: 3165 g vs 3118 g Premature contractions: <i>n</i> =6 vs <i>n</i> =3, 1.9 [0.4-8.8] Maternal morbidity: no
Buser ⁵⁶	A single-center retrospective case series study	Pregnant women, pregnancies <i>n</i> =2783 Study period: 1995-2007	Women with non-obstetric LS surgery <i>n</i> =36, procedures <i>n</i> =37 (1.3%) First trimester <i>n</i> =8, second <i>n</i> =22, third <i>n</i> =7	Fetal loss, PB, maternal complications	No fetal loss PB: <i>n</i> =1 Intraoperative uterus perforation <i>n</i> =1 • Cholecystectomy <i>n</i> =27 • Appendectomy <i>n</i> =9 • Other <i>n</i> =1
McGory et al. ¹⁰	A retrospective, nationwide registry-based cohort study	Pregnant women with appendectomy <i>n</i> =3133 Study period: 1995-2002	Appendectomy <i>n</i> =3133: LS <i>n</i> =454 (14%), open <i>n</i> =2679 (86%)	Fetal loss, PB	OR LS vs open surgery: Fetal loss: <i>n</i> =31 (6.8%) vs <i>n</i> =88 (2.8%), 2.2 [1.4-3.3] PB: <i>n</i> =1 (<1%) vs 216 (8.1%), 0.1 [0.1-0.2]
Carver et al. ⁵⁷	A single-center, retrospective cohort study	Pregnant women with appendectomy <i>n</i> =28 Study period: 2001-2002	Appendectomy <i>n</i> =28 LS <i>n</i> =17 (first trimester <i>n</i> =5, second <i>n</i> =12) Open <i>n</i> =11 (first <i>n</i> =4, second <i>n</i> =7)	MC, fetal loss, PB, BW, premature contractions, developmental delays	OR LS vs open surgery: MC: <i>n</i> =2 vs <i>n</i> =0, 3.7 [0.2-84.9] Fetal loss: none PB: none BW: 3500 g vs 3500 g Premature contractions: <i>n</i> =0 vs <i>n</i> =1, 0.2 [0.1-5.4] Developmental delays: no
Rojansky et al. ⁵⁸	A single-center retrospective cohort study	Pregnant women with abdominal surgery, <i>n</i> =43 Study period: 1990-1999	Abdominal surgery, <i>n</i> =43 LS <i>n</i> =21 Open <i>n</i> =22	MC, fetal loss, PB, BW, SGA, Apgar score <7, congenital malformation, premature contractions, maternal morbidity	OR LS vs open surgery: MC: <i>n</i> =1 vs <i>n</i> =2, 0.5 [0.1-6.0] Fetal loss: no PB: <i>n</i> =0 vs <i>n</i> =3, 0.1 [0.1-2.7] BW: 3265 g vs 2878 g SGA: <i>n</i> =0 vs <i>n</i> =5, 0.1 [0.1-1.4] Apgar score <7: no Congenital malformation: <i>n</i> = <i>n</i> =1 vs <i>n</i> =1, 1.1 [0.1-18.3] Premature contractions: <i>n</i> =0 vs <i>n</i> =5, 0.1 [0.1-1.4] Postoperative bleeding: <i>n</i> =1 vs <i>n</i> =0, 3.3 [0.1-87.5] • Appendectomy: LS <i>n</i> =13, open <i>n</i> =12 • Other surgery: LS <i>n</i> =5, open <i>n</i> =7
Lee et al. ⁵⁹	A single-center retrospective cross-sectional study	Pregnant women with ovarian tumors, <i>n</i> =101 Study period: 1990-2001	Surgery for ovarian tumors, <i>n</i> =101, analyzed <i>n</i> =89 Emergent surgery <i>n</i> =36 (first trimester <i>n</i> =22, second <i>n</i> =5, third <i>n</i> =9) Elective surgery <i>n</i> =53 (first <i>n</i> =18, second <i>n</i> =35)	PB, BW, neonatal mortality	OR emergent vs elective surgery: PB: <i>n</i> =8 vs <i>n</i> =2, 7.3 [1.4-36.7] BW: 3080 g vs 3170 g Neonatal mortality: no

(Continued)

Table 2. (Continued)

Publication information	Study design	Participants, time	Surgery	Outcome measures	Main results
Jenkins et al. ⁶⁰	A two-center retrospective cohort study	Pregnant women <i>n</i> = 69,800 Study period: 1989-1999	Non-obstetric surgery <i>n</i> = 215 (0.3%), analyzed <i>n</i> = 116 First trimester <i>n</i> = 28, second <i>n</i> = 62, third <i>n</i> = 26	Fetal loss, PB, maternal morbidity	Fetal loss: <i>n</i> = 1 PB: <i>n</i> = 20 (21%) Wound infection: <i>n</i> = 1 <ul style="list-style-type: none"> Ovarian cystectomy/oophorectomy: <i>n</i> = 39 (34%) Appendectomy: <i>n</i> = 19 (16%) Cholecystectomy: <i>n</i> = 11 (9%)
Muench et al. ⁶¹	A single-center retrospective cohort study	Pregnant women with LS cholecystectomy <i>n</i> = 16 Study period 1992-1999	LS cholecystectomy <i>n</i> = 16 (converted <i>n</i> = 2) First trimester <i>n</i> = 3, second <i>n</i> = 11, third <i>n</i> = 2	PB, Apgar score < 7, neonatal morbidity, neonatal mortality, maternal morbidity, maternal mortality	PB: <i>n</i> = 1 Apgar score < 7: <i>n</i> = 1 Neonatal morbidity: no Neonatal mortality: no Maternal morbidity: no Maternal mortality: no Premature contraction: <i>n</i> = 4
Sakhri et al. ⁶²	A single-center, retrospective cohort study	Pregnant women <i>n</i> = 55,197 Study period: 1991-1998	Appendectomy <i>n</i> = 23 (0.04%) First trimester <i>n</i> = 2, second <i>n</i> = 6, third <i>n</i> = 15	Fetal loss, PB, LBW, Apgar score < 7, maternal morbidity	Fetal loss: <i>n</i> = 1 PB: <i>n</i> = 3 LBW: <i>n</i> = 3 Apgar score < 7: <i>n</i> = 3 Premature contraction: <i>n</i> = 3 Wound infection: <i>n</i> = 2 Pulmonary atelectasis: <i>n</i> = 2
Lyass et al. ⁶³	A single-center case control prospective study	Pregnant women with appendectomy <i>n</i> = 22 Study period 1996-1999	Appendectomy <i>n</i> = 22 LS 11 (first <i>n</i> = 5, second <i>n</i> = 4, third <i>n</i> = 2) Open <i>n</i> = 11 (first trimester <i>n</i> = 2, second <i>n</i> = 4, third <i>n</i> = 5)	Fetal loss, PB, developmental delays, maternal morbidity	LS vs open surgery: Fetal loss: no PB: no Developmental delays: no Maternal morbidity: no Premature contraction: <i>n</i> = 1 vs <i>n</i> = 1, 1.0 [0.1-18.3]
Hsu et al. ⁶⁴	A single-center, retrospective cohort study	Pregnant women, <i>n</i> = 52,894 Study period: 1991-1997	Appendectomy <i>n</i> = 45 (0.09%)	Fetal loss, maternal morbidity	Fetal loss: <i>n</i> = 4 (elective abortion <i>n</i> = 3) Wound infection/abscess: <i>n</i> = 6
Gerstenfeld et al. ⁶⁵	A single-center retrospective cohort study	Pregnant women <i>n</i> = 56,305 Study period: 1991-1998	Non-obstetrical abdominal surgery <i>n</i> = 106: LS <i>n</i> = 18, Open <i>n</i> = 88 Emergent: <i>n</i> = 73 Elective <i>n</i> = 31 First trimester <i>n</i> = 53, second <i>n</i> = 52, third <i>n</i> = 1	MC, PB, BW, LBW, Apgar score < 7	Surgery vs control deliveries: MC: <i>n</i> = 2 PB: <i>n</i> = 11 (18%) vs <i>n</i> = 8999 (16%), OR 1.1 [0.6-2.2] BW: 3331 g LBW: <i>n</i> = 6 (9.8%) vs <i>n</i> = 4836 (8.6%), OR 1.2 [0.5-2.7] Apgar score < 7: 0 vs 0 <ul style="list-style-type: none"> Adnexal mass/torsion 59% Appendicitis 31% Cholelithiasis 6% Myoma 3%
Mourad et al. ⁶⁶	A single-center retrospective study	Pregnant women, deliveries <i>n</i> = 66,993 Study period 1986-1995	Appendectomy <i>n</i> = 67 (0.1%) First trimester <i>n</i> = 17, second <i>n</i> = 27, third <i>n</i> = 23	PB, premature contractions	PB: <i>n</i> = 3 Premature contractions: <i>n</i> = 19
Usui et al. ⁶⁷	A single-center retrospective cohort study	Pregnant women <i>n</i> = 15,304 Study period 1980-1997	Women with adnexal mass <i>n</i> = 69 (0.5%) Laparotomy <i>n</i> = 68 Needle aspiration <i>n</i> = 1	MC, fetal loss, PB, BW, neonatal mortality	MC: <i>n</i> = 2 Fetal loss: <i>n</i> = 1 PB: <i>n</i> = 7 BW: 3124 g Neonatal mortality: <i>n</i> = 2
Tracey and Fletcher ⁶⁸	A single-center retrospective cohort study	Pregnant women, deliveries <i>n</i> = 44,845 Study period: 1991-1998	Appendectomy <i>n</i> = 22 (< 0.1%): LS = 3 (first trimester <i>n</i> = 3) Open <i>n</i> = 19 (first <i>n</i> = 2, second <i>n</i> = 6, third <i>n</i> = 11)	Fetal loss, PB, maternal morbidity	Fetal loss: no PB: <i>n</i> = 5 Premature contractions: <i>n</i> = 6 Wound infection/sepsis: <i>n</i> = 3 Ileus/bowel obstruction: <i>n</i> = 2

aRR: adjusted risk ratio; ARDS: adult respiratory distress syndrome; BW: birth weight; CI: confidence interval; CNS: central nervous system; EENT: eye, ear, nose and throat; ERCP: endoscopic retrograde cholangiopancreatography; FESS: functional endoscopic sinus surgery; GA: gestational age; GW: gestational week; HR: hazard ratio; LS: laparoscopic surgery; LBW: low birth weight; MC: miscarriage; OR: odds ratio; PB: premature birth; RR: risk ratio; SGA: small for gestational age.

were data for 47,153 pregnant women; 43% of procedures were carried out during the first, 32% during the second, and 25% during the third trimester.

Description of the studies according to the fetal and maternal outcomes

Miscarriage. Data for miscarriage (fetal loss before 20 weeks of pregnancy) were reported in 25 studies.^{13,16–18,21,23–25,29,34–37,40,41,46,48,51–53,55,57,58,65,67} In the majority of these studies gestational age at surgery was reported, and the timing of the intervention being in the early pregnancy was verified. The prevalence of miscarriage was 3.9% in pregnancies where the mother had non-obstetric surgery ($n=54,223$). Most of the studies provided data on time from surgery to the event of miscarriage, which was most commonly within the first two weeks after surgery. In four studies comparing outcomes after non-obstetric surgery ($n=52,615$) with no surgery/conservative treatment ($n=7,773,465$), the prevalence of miscarriage was similar at 5.1% and 4.6%, with an OR of 1.1 [95% CI 1.1–1.2].^{23,29,34,35} Based on data from nine studies ($n=693$) comparing outcomes after laparoscopic and open non-obstetric surgery, the prevalence of miscarriage was 4.7% and 2.6%, with an OR of 1.9 [0.81–4.3], respectively.^{36,37,41,46,52,53,55,57,58}

Stillbirth. Stillbirth (fetal loss at or after 20 weeks of pregnancy) is another concern associated with non-obstetric surgery during pregnancy. Data for stillbirth were reported in 35 studies.^{10–12,16,20,21,25,26,28,31,32,35,36,38–42,44,45,47,49,52–54,56–58,60,62–64,67–69} The prevalence of stillbirth in pregnancies where the mother had non-obstetric surgery ($n=67,649$) was 1.1%. In 6 studies comparing outcomes after non-obstetric surgery ($n=58,642$) with no surgery/conservative treatment ($n=8,791,416$), the prevalence of stillbirth was higher in pregnancies with surgery at 1.3% than in pregnancies with no surgery at 0.5%, with an OR of 2.0 [1.9–2.2].^{11,12,26,30,31,42} Based on data from 16 studies comparing outcomes after laparoscopic ($n=979$) and open ($n=3781$) non-obstetric surgery, the prevalence of stillbirth was slightly higher at 4.5% after laparoscopic surgery than after open surgery at 3.5%, with an OR of 1.3 [0.9–1.8].^{10,28,32,36,38,39,41,45,52–54,57,58,63,68,69}

Preterm birth. Preterm birth (birth before 37 weeks of pregnancy) was the most commonly reported outcome, reported in 54 studies.^{10–17,19–39,41–46,48,50–54,56–63,65–69} There were 8265 (9.7%) preterm births in 67,367 pregnancies in women with non-obstetric surgery. Fourteen studies compared data on preterm births in women with non-obstetric surgery ($n=73,110$) and with no surgery during pregnancy ($n=14,833,865$). The prevalence of preterm birth was higher in women with non-obstetric surgery, 9.8% versus 4.9%, with an OR of 2.1 [2.0–2.1].^{11,12,15,23,25,26,29,33–35,43,45,50,65} Based on data from 22 studies comparing outcomes after laparoscopic ($n=4730$) and open ($n=9477$) non-obstetric surgery, the prevalence of preterm birth was lower at 4.8% after

laparoscopic surgery than after open surgery at 7.0%, with an OR of 0.68 [0.58–0.79].^{10,15,21,26,28,30,32,36–39,41,45,46,48,52–54,57,58,63,69}

Low birth weight. Data on low birth weight and on fetuses being small for gestational age were reported in 19 studies.^{12–16,19,22,23,25–27,33–35,50,53,58,62,65} The prevalence of low birth weight was 7.8% in 64,329 pregnancies and that of fetuses being small for gestational age was 6.5% in 6980 pregnancies in which non-obstetric surgery was performed. Seven studies compared low birth weight between deliveries in women who had undergone non-obstetric surgery during pregnancy ($n=61,762$) and women with no surgery ($n=9,822,477$). The prevalence of low birth weight was higher after pregnancies in which surgery was performed at 8.0% versus 4.7%, with an OR of 1.8 [1.7–1.8].^{12,15,25,34,35,50,65} On the contrary, non-obstetric surgery did not have an impact on the prevalence of fetuses being small for gestational age. In four studies comparing that aspect, the prevalence was 6.6% ($n=6661$) in pregnancies in which non-obstetric surgery was performed and 6.0% ($n=2,328,110$) in pregnancies with no surgery, OR 1.1 [1.0–1.2], respectively.^{23,26,33,50} In Cho et al.¹⁵ study, the prevalence of low birth weight was 5.6% after laparoscopic and 5.8% after open surgery. The prevalence of small for gestational age was 7.0% after laparoscopic surgery ($n=640$) and 9.2% after open surgery ($n=521$), with an OR of 0.7 [0.5–1.1].^{26,53,58}

Low 5 min Apgar score. Data on a low Apgar score of < 7 at 5 min were reported in 16 studies.^{12,14,17,19,22,26,27,33,37,43,50,58,61,62,65} The prevalence of a low Apgar score was 1.7% in 9822 pregnancies in which non-obstetric surgery was performed. Six studies compared low Apgar scores between deliveries in women who had undergone surgery during pregnancy ($n=7,085$) with women with no surgery ($n=1,205,005$), and the prevalence was similar at 2.1% versus 1.9%, with an OR of 1.1 [0.9–1.3].^{12,26,33,43,50,65}

Six studies reported the prevalence of low Apgar scores after laparoscopic ($n=655$) and open surgery ($n=610$), and the prevalence was 1.2% and 2.6%, respectively, with an OR of 0.50 [0.2–1.1].^{26,27,37,58,61,65}

Developmental delays or congenital anomalies. Data on developmental delays were reported in three studies,^{49,57,63} and data on congenital anomalies were reported in eight studies.^{11,14,17,18,32,50,51,58} There were no cases of developmental delays. Non-obstetric surgery ($n=5453$) did not affect the prevalence of congenital anomalies, the prevalence was 4.1% in both groups.

Maternal morbidity or mortality. Data on maternal morbidity or mortality were available in 36 studies.^{11,16,17,20,21,24,26–33,35,37–42,46,48,49,52,54–58,60–64,68,69} The maternal mortality rate reported in eleven studies was 0.029% in pregnancies in which

non-obstetric surgery was performed ($n=52,255$) and 0.0043% in women with no surgery during pregnancy ($n=7,728,427$), with an OR of 6.6 [4.0-11.1].^{11,16,17,20,21,24,29,35,40,48,56,61} Data on postoperative maternal morbidity were inconsistent. A detailed listing of complications was provided in four studies.^{42,46,62,68} There were no data on the type of morbidity in four studies.^{24,26,31,33} Surgical site infection/fever ($n=43$) was reported in 17 studies,^{17,18,27,28,30,32,37-39,41,48,49,52,54,60,64,69} and postoperative hemorrhage/hemoperitoneum was reported in two studies.^{54,58} There was no maternal morbidity related to non-obstetric surgery in four studies.^{55,57,61,63}

Discussion

This systematic review identified 60 studies published between January 2000 and November 2022 that provided eligible data concerning pregnancy, fetal and maternal outcomes after non-obstetric surgery during pregnancy. Most of the data in these publications were from the last two decades, and some older data from the 1980s were reported in three publications.⁶⁰⁻⁶⁷ The review included data for 80,205 women who underwent non-obstetric surgery during pregnancy and data for 16,655,486 pregnancies in women who had no surgery during pregnancy.

The prevalence of non-obstetric surgery was between 0.23% and 0.74% (median 0.37%), which is substantially less than the commonly quoted 2% based on data from the 1960s⁷⁰ and the 1.6% recently reported in Denmark.⁷¹ The median proportions for the trimesters of non-obstetric surgeries were 43% for the first, 32% for the second, and 25% for the third trimester. In this review, the proportion was higher in the first trimester and lower in the second trimester than those at 30% and 50% reported by Cohen-Kerem et al.⁷² in the earlier review. Regarding emergent surgery, the distribution between the trimesters was more equal.

In our review, pregnant women who underwent non-obstetric surgery during pregnancy had an increased rate of stillbirth (OR 2.0), preterm birth (OR 2.1), and low birth weight (OR 1.8) compared to pregnant women with no non-obstetric surgery during pregnancy. However, surgery during pregnancy did not increase the rate of miscarriage (OR 1.1), low 5 min Apgar scores (OR 1.1), congenital anomalies (OR 1.0) or fetuses being small for gestational age (OR 1.1). The latter indicates that non-obstetric surgery during pregnancy was not associated with intrauterine growth retardation and that the higher prevalence of preterm births is the likely reason for the higher prevalence of low birth weight for women who underwent surgery.

Our data are consistent with that of older studies showing that non-obstetric surgery may increase the risk of adverse pregnancy outcomes.^{1,70,72} The prevalence of miscarriage (3.9% vs 5.8%), fetal loss (1.1% vs 2.0%) and maternal mortality rate in women (0.029% vs 0.053%) in our data were substantially less than, birth defects (4.1% vs 2.0%) higher, and prematurity similar (9.7% vs 8.2%) to that earlier review

by Cohen-Kerem et al.,⁷² Of note, the prevalence of birth defects in the present review was similar in neonates after pregnancy with non-obstetric surgery and after pregnancy with no surgery. Recently, Moore et al.⁷³ showed that the 30-day mortality rates are similar in pregnant women and non-pregnant women undergoing general surgery. However, in that study,⁷³ the mortality rate was 10-fold higher at 0.3%-0.4% compared to the studies in this review. Taken together, our systematic review indicates that the maternal and fetal safety of non-obstetric surgery during pregnancy have increased during the last two decades, but that it is still associated increased rates of stillbirth and preterm birth. It remains an open question whether these risks are related to surgical procedures *per se*, the surgical disease treated, or a combination of both.

Abdominal surgery was the most common emergent surgery in the present review, and appendectomy was the most common single procedure with a median rate of 98/100,000 pregnant women. In this review, there were no studies comparing surgical approach with non-surgical treatment to treat acute appendicitis during pregnancy. In the non-pregnant population, antibiotic treatment is increasingly used as an alternative to surgery for uncomplicated acute appendicitis.⁷⁴ Recently, Yang et al.⁷⁵ showed that antibiotic treatment could be a feasible treatment for acute appendicitis in pregnant women also.

Cholecystectomy was also a common procedure with a median surgery rate of 21/100,000 pregnant women. This is consistent with data indicating that pregnant women are at higher risk of gallstones and associated diseases, such as cholecystitis, cholangitis, and pancreatitis. In this review, two studies compared operative and non-operative treatment and showed rather similar outcomes for these two approaches, but the surgical cases had a higher prevalence of low Apgar scores (4.2% vs 1.8%) compared to women who received non-operative treatment.^{33,34} Regarding cholecystectomy, the laparoscopic approach was used in most of the surgical cases, but the conversion rate was relatively high (14%), 3-fold higher than reported in non-pregnant population.⁷⁶ Minilaparotomy is another mini-invasive surgical cholecystectomy technique,⁷⁶ but no data on pregnant women were available.

Contrary to what was expected, our review shows no increase in the proportion of the laparoscopic approach over time for abdominal cavity surgery. Thirty-two studies including 36,000 pregnant women showed equal proportions regarding the use of the two techniques; 47% of patients had laparoscopic surgery and 53% had open surgery. The even prevalence of the laparoscopic approach was not expected, as the popularity of laparoscopic surgeries has increased over the last decades in surgical populations in general.⁷⁷ In 2011, the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons stated that laparoscopic treatment of acute abdominal disease has the same indications in pregnant and nonpregnant patients, and that laparoscopy can be safely performed during all trimesters of

pregnancy.⁷⁸ In the present review, the laparoscopic approach was used in four out of five cases in the first trimester, but only in one out of four abdominal procedures in the third trimester. Pregnant patients undergoing laparoscopic surgery had a two-fold higher rate of miscarriage and a one-third-fold higher rate of stillbirth, but a substantially lower rate of preterm birth, the fetus being small for gestational age, and low 5 min Apgar scores compared to open surgery. This is consistent with previous systematic reviews reporting that laparoscopy is associated with a higher rate of fetal loss, but a lower risk of preterm birth compared to open surgery.^{79,80}

Not only surgical disease and surgery but also anesthetic agents are a concern in non-obstetric surgery during pregnancy. In clinical situations, it is difficult to separate the effects of anesthesia from those of surgery. Concerns about anesthetic effects were raised again two decades ago when experimental data showed that exposure to anesthetic agents may cause widespread neurodegeneration in the developing brain, as well as persistent memory and learning impairments.⁸¹ However, in animal studies, a number of confounding variables make these conclusions difficult to interpret for a human population. Human data have not shown these kinds of harmful effects on the developing fetal brain, and currently used anesthetics have not been shown to be teratogenic in clinical concentrations.²

The surgical condition itself can be a potential risk for pregnant women, pregnancy outcomes, and fetuses if left untreated. Therefore, the need for surgery and the timing of the intervention must be carefully evaluated. However, half of the procedures in the present studies were scheduled, indicating that non-emergent surgery is still common in pregnant women.^{24,29,35,59,65} One study comparing pregnancy outcomes after emergent and scheduled surgery found that emergency surgery was associated with a higher risk of preterm birth.⁵⁹ Moreover, studies in which the majority of the surgeries were emergent the rate of adverse birth outcomes were similar compared to pregnant women with no surgery.^{24,65}

Our study provides an updated systematic review that evaluates the effects of non-obstetric surgery during pregnancy on pregnancy, fetal and maternal outcomes, and on adherence to recent guidelines.^{2,3,13} The main limitation of this systematic review is that all the data, except one small study,⁶³ were based on retrospective studies. Furthermore, less than half of the studies had a control group consisting of pregnant women with no non-obstetric surgery during pregnancy. One of the main limitations is the heterogeneity of the types of non-obstetric surgery included in the publications. We assume that the risks for the pregnancy, fetal and maternal outcomes are not the same for example elective dental procedures and emergent abdominal cavity surgery.³⁵ This heterogeneity should be taken into account when interpreting the data of the present review. It appeared that only a few publications^{11,24,29,35,59,65} provide data on whether the procedures were elective or emergent, and even less data was available for the distribution on surgical diagnoses on benign

or malignant conditions. Thus, we feel unable to give any evidence-based recommendations for performing elective surgical procedures during pregnancy and to conclude whether any specific trimester is safe from this point of view.

Further investigation is also needed concerning the comparison of conservative and operative approaches in managing different diseases in pregnant women. For example, many studies have shown the safety of surgical treatment for acute appendicitis,^{24,27,30} but no data are available comparing surgery and conservative treatment for pregnant women with this condition.

In conclusion, non-obstetric surgery during pregnancy increases the risk of stillbirth, preterm birth, and congenital anomalies. Surgical disease itself, however, can be a potential risk for pregnancy, fetus, and pregnant woman, and therefore surgical intervention should not be postponed in emergent conditions requiring surgery. Furthermore, our study demonstrates that the fetal and maternal safety of non-obstetric surgery have increased during the last two decades, and that both the laparoscopic and open techniques are feasible for pregnant women.

Author contributions

The concept or design of the work: AH, HK, OU, MK; Acquisition and analysis of data: AH, HK; Interpretation of data: AH, HK, OU, MK; Drafted the article: AH; Revised it critically for important intellectual content: HK, OU, MK; Approved the version to be published: AH, HK, OU, MK.

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ORCID iD

Merja Kokki  <https://orcid.org/0000-0003-1501-7537>

Supplemental material

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References

1. Brodsky JB, Cohen EN, Brown BW et al: Surgery during pregnancy and fetal outcome. *Am J Obstet Gynecol* 1980;138:1165–1167.
2. ACOG Committee Opinion No. 775: Nonobstetric surgery during pregnancy. *Obstet Gynecol* 2019;133:e285–e286.
3. Jalonen J, Kokki H, Hynynen M et al. Leikkausta edeltävä arviointi [Update on current care guidelines: Preoperative evaluation]. *Duodecim* 2014;130:1768–1769 (in Finnish).
4. Duncan PG, Pope WD, Cohen MM et al: Fetal risk of anesthesia and surgery during pregnancy. *Anesthesiology* 1986;64(6):790–794.

5. Mazze RI, Källén B: Reproductive outcome after anesthesia and operation during pregnancy: A registry study of 5405 cases. *Am J Obstet Gynecol* 1989;161(5):1178–1185.
6. Bleeser T, Van Der Veeken L, Fieuws S et al: Effects of general anaesthesia during pregnancy on neurocognitive development of the fetus: A systematic review and meta-analysis. *Br J Anaesth* 2021;126(6):1128–1140.
7. Reedy MB, Källén B, Kuehl TJ: Laparoscopy during pregnancy: A study of five fetal outcome parameters with use of the Swedish Health Registry. *Am J Obstet Gynecol* 1997;177(3):673–679.
8. Page MJ, McKenzie JE, Bossuyt PM et al: The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
9. Murad MH, Sultan S, Haffar S et al: Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med* 2018;23(2):60–63.
10. McGory ML, Zingmond DS, Tillou A et al: Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss. *J Am Coll Surg* 2007;205(4):534–540.
11. Haataja A, Gissler M, Kokki H et al: Nonobstetric surgery during pregnancy in Finland during a 21-year period: A register-based study. *Reprod Female Child Health* 2022;1:51–61.
12. Fu P-H, Yu C-H, Chen Y-C et al: Risk of adverse fetal outcomes following nonobstetric surgery during gestation: A nationwide population-based analysis. *BMC Pregnancy Childbirth* 2022;22:406.
13. Chwat C, Terres M, Duarte MR et al: Laparoscopic treatment for appendicitis during pregnancy: Retrospective cohort study. *Ann Med Surg* 2021;68:102668.
14. Torres SM, Duarte DF, Glória AS et al: Sugammadex administration in pregnant patients undergoing non-obstetric surgery: A case series. *Braz J Anesthesiol* 2022;72(4):525–528.
15. Cho HW, Cho GJ, Noh E et al: Pregnancy outcomes following laparoscopic and open surgery in Pelvis during pregnancy: A nationwide population-based study in Korea. *J Korean Med Sci* 2021;36:e192.
16. Choi HN, Ng BRJ, Arafat Y et al: Evaluation of safety and foeto-maternal outcome following non-obstetric surgery in pregnancy: A retrospective single-site Australian study. *ANZ J Surg* 2021;91(4):627–632.
17. Tanridan Okcu N, Cesur IB, İrkörücü O: Acute appendicitis in pregnancy: 50 case series, maternal and neonatal outcomes. *Ulus Travma Acil Cerrahi Derg* 2021;27:255–259.
18. Cho IS, Bae SU, Jeong WK et al: Single-port laparoscopic appendectomy for acute appendicitis during pregnancy. *J Minim Access Surg* 2021;17(1):37–42.
19. Xiao J, Fu K, Duan K et al: Pregnancy-preserving laparoscopic single-site surgery for gynecologic disease: A case series. *J Minim Invasive Gynecol* 2020;27(7):1588–1597.
20. Moffatt SE, Goldberg B, Kong VY et al: Trauma in pregnancy at a major trauma centre in South Africa. *S Afr Med J* 2020;110:667–670.
21. Cho S, Chung RK, Jin SH: Factors affecting maternal and fetal outcomes of non-obstetric surgery and anesthesia during pregnancy: A retrospective review of data at a single Tertiary University Hospital. *J Korean Med Sci* 2020;35:e113.
22. Buitrago G, Arevalo K, Moyano JS et al: Appendectomy in third trimester of pregnancy and birth outcomes: A propensity score analysis of a 6-year cohort study using administrative claims data. *World J Surg* 2020;44(1):12–20.
23. Rasmussen AS, Christiansen CF, Ulrichsen SP et al: Non-obstetric abdominal surgery during pregnancy and birth outcomes: A Danish registry-based cohort study. *Acta Obstet Gynecol Scand* 2020;99(4):469–476.
24. Vujic J, Marsoner K, Lipp-Pump AH et al: Non-obstetric surgery during pregnancy—An eleven-year retrospective analysis. *BMC Pregnancy Childbirth* 2019;19:382.
25. Devroe S, Bleeser T, Van de Velde M et al: Anesthesia for non-obstetric surgery during pregnancy in a tertiary referral center: A 16-year retrospective, matched case-control, cohort study. *Int J Obstet Anesth* 2019;39:74–81.
26. Ibiebele I, Schnitzler M, Nippita T et al: Appendectomy during pregnancy and the risk of preterm birth: A population data linkage study. *Aust N Z J Obstet Gynaecol* 2019;59(1):45–53.
27. Cohen SB, Wadat H, Shapira M et al: Urgent laparoscopic surgeries during the third trimester of pregnancy: A case series. *J Minim Invasive Gynecol* 2020;27(4):909–914.
28. Gök AFK, Soydaş Y, Bayraktar A et al: Laparoscopic versus open appendectomy in pregnancy: A single center experience. *Ulus Travma Acil Cerrahi Derg* 2018;24(6):552–556.
29. Yu CH, Weng SF, Ho CH et al: Pregnancy outcomes following nonobstetric surgery during gestation: A nationwide population-based case-control study in Taiwan. *BMC Pregnancy Childbirth* 2018;18:460.
30. Kwon H, Lee M, Park HS et al: Laparoscopic management is feasible for nonobstetric surgical disease in all trimesters of pregnancy. *Surg Endosc* 2018;32(6):2643–2649.
31. Won RP, Friedlander S, Lee SL: Management and outcomes of appendectomy during pregnancy. *Am Surg* 2017;83:1103–1107.
32. Alkatary MM, Bahgat NA: Laparoscopic versus open appendectomy during pregnancy. *Int Surg J* 2017;48:2387–2391.
33. Ibiebele I, Schnitzler M, Nippita T et al: Outcomes of gallstone disease during pregnancy: A population-based data linkage study. *Paediatr Perinat Epidemiol* 2017;31(6):522–530.
34. Hedström J, Nilsson J, Andersson R et al: Changing management of gallstone—related disease in pregnancy—A retrospective cohort analysis. *Scand J Gastroenterol* 2017;52(9):1016–1021.
35. Aylin P, Bennett P, Bottle A et al: Estimating the Risk of Adverse Birth Outcomes in Pregnant Women Undergoing Non-Obstetric Surgery Using Routinely Collected NHS Data: An Observational Study. NIHR Journals Library, Southampton, 2016.
36. Winter NN, Guest GD, Bozin M et al: Laparoscopic or open appendectomy for suspected appendicitis in pregnancy and evaluation of foetal outcome in Australia. *ANZ J Surg* 2017;87:334–338.
37. Segev L, Segev Y, Rayman S et al: Appendectomy in pregnancy: Appraisal of the minimally invasive approach. *J Laparoendosc Adv Surg Tech A* 2016;26(11):893–897.
38. Laustsen JF, Bjerring OS, Johannessen Ø et al: Laparoscopic appendectomy during pregnancy is safe for both the mother and the fetus. *Dan Med J* 2016;63:A5259.
39. Yoo KC, Park JH, Pak KH et al: Could laparoscopic appendectomy in pregnant women affect obstetric outcomes? A multicenter study. *Int J Colorectal Dis* 2016;31(8):1475–1481.
40. Shambe IH, Dikkol N, Ozoilo KN: Pregnancy outcome following non-obstetric abdominal surgery in Jos University Teaching Hospital: A 5-year retrospective study. *Niger J Clin Pract* 2016;19(5):591–594.
41. Karaman E, Aras A, Çim N et al: Maternal and fetal outcomes after laparoscopic vs. open appendectomy in pregnant women: Data from two tertiary referral centers. *Ginekol Pol* 2016;87(2):98–103.

42. Paramanathan A, Walsh SZ, Zhou J et al: Laparoscopic cholecystectomy in pregnancy: An Australian retrospective cohort study. *Int J Surg* 2015;18:220–223.
43. Schwarzman P, Baumfeld Y, Bar-Niv Z et al: The effect of non-obstetric invasive procedures during pregnancy on perinatal outcomes. *Arch Gynecol Obstet* 2015;292(3):603–608.
44. Baldwin EA, Borowski KS, Brost BC et al: Antepartum nonobstetrical surgery at ≥ 23 weeks' gestation and risk for preterm delivery. *Am J Obstet Gynecol* 2015;212(2):232.e1–232.e5.
45. Cheng HT, Wang YC, Lo HC et al: Laparoscopic appendectomy versus open appendectomy in pregnancy: A population-based analysis of maternal outcome. *Surg Endosc* 2015;29(6):1394–1399.
46. Peled Y, Hiersch L, Khalpari O et al: Appendectomy during pregnancy—Is pregnancy outcome depending by operation technique? *J Matern Fetal Neonatal Med* 2014;27(4):365–367.
47. Fardiazar Z, Derakhshan I, Torab R et al: Maternal-neonatal outcome in pregnancies with non-obstetric laparotomy during pregnancy. *Pak J Biol Sci* 2014;17:260–265.
48. Jung SJ, Lee DK, Kim JH et al: Appendicitis during pregnancy: The clinical experience of a secondary hospital. *J Korean Soc Coloproctol* 2012;28(3):152–159.
49. Choi JJ, Mustafa R, Lynn ET et al: Appendectomy during pregnancy: Follow-up of progeny. *J Am Coll Surg* 2011;213(5):627–632.
50. Wei PL, Keller JJ, Liang HH et al: Acute appendicitis and adverse pregnancy outcomes: A nationwide population-based study. *J Gastrointest Surg* 2012;16(6):1204–1211.
51. Hannan MJ, Hoque MM, Begum LN: Laparoscopic appendectomy in pregnant women: Experience in Chittagong, Bangladesh. *World J Surg* 2012;36(4):767–770.
52. Eom JM, Hong JH, Jeon SW et al: Safety and clinical efficacy of laparoscopic appendectomy for pregnant women with acute appendicitis. *Ann Acad Med* 2012;41(2):82–86.
53. Corneille MG, Gallup TM, Bening T et al: The use of laparoscopic surgery in pregnancy: Evaluation of safety and efficacy. *Am J Surg* 2010;200(3):363–367.
54. Sadot E, Telem DA, Arora M et al: Laparoscopy: A safe approach to appendicitis during pregnancy. *Surg Endosc* 2010;24(2):383–389.
55. Kirshtein B, Perry ZH, Avinoach E et al: Safety of laparoscopic appendectomy during pregnancy. *World J Surg* 2009;33:475–480.
56. Buser KB: Laparoscopic surgery in the pregnant patient: Results and recommendations. *JLS* 2009;13:32–35.
57. Carver TW, Antevil J, Egan JC et al: Appendectomy during early pregnancy: What is the preferred surgical approach? *Am Surg* 2005;71(10):809–812.
58. Rojansky N, Shushan A, Fatum M: Laparoscopy versus laparotomy in pregnancy: A comparative study. *J Am Assoc Gynecol Laparosc* 2002;9(1):108–110.
59. Lee GS, Hur SY, Shin JC et al: Elective vs. conservative management of ovarian tumors in pregnancy. *Int J Gynaecol Obstet* 2004;85(3):250–254.
60. Jenkins TM, Mackey SF, Benzoni EM et al: Non-obstetric surgery during gestation: Risk factors for lower birthweight. *Aust N Z J Obstet Gynaecol* 2003;43(1):27–31.
61. Muench J, Albrink M, Serafini F et al: Delay in treatment of biliary disease during pregnancy increases morbidity and can be avoided with safe laparoscopic cholecystectomy. *Am Surg* 2001;67(6):539–542; discussion 542–543.
62. Sakhri J, Youssef S, ben Letaifa D et al: Les appendicites aigues au cours de la grossesse [Acute appendicitis during pregnancy]. *Tunis Med* 2001;79:521–525 (in French).
63. Lyass S, Pikarsky A, Eisenberg VH et al: Is laparoscopic appendectomy safe in pregnant women? *Surg Endosc* 2001;15:377–379.
64. Hsu YP, Chen RJ, Fang JF et al: Acute appendicitis during pregnancy: A clinical assessment. *Chang Gung Med J* 2001;24(4):245–250.
65. Gerstenfeld TS, Chang DT, Pliego AR et al: Nonobstetrical abdominal surgery during pregnancy in Women's Hospital. *J Matern Fetal Med* 2000;9(3):170–172.
66. Mourad J, Elliott JP, Erickson L et al: Appendicitis in pregnancy: New information that contradicts long-held clinical beliefs. *Am J Obstet Gynecol* 2000;182(5):1027–1029.
67. Usui R, Minakami H, Kosuge S et al: A retrospective survey of clinical, pathologic, and prognostic features of adnexal masses operated on during pregnancy. *J Obstet Gynaecol Res* 2000;26(2):89–93.
68. Tracey M, Fletcher HS: Appendicitis in pregnancy. *Am Surg* 2000;66:555–560.
69. Chung JC, Cho GS, Shin EJ et al: Clinical outcomes compared between laparoscopic and open appendectomy in pregnant women. *Can J Surg* 2013;56(5):341–346.
70. Shnider SM, Webster GM: Maternal and fetal hazards of surgery during pregnancy. *Am J Obstet Gynecol* 1965;92:891–900.
71. Rasmussen AS, Christiansen CF, Uldbjerg N et al: Obstetric and non-obstetric surgery during pregnancy: A 20-year Danish population-based prevalence study. *BMJ Open* 2019;9:e028136.
72. Cohen-Kerem R, Railton C, Oren D et al: Pregnancy outcome following non-obstetric surgical intervention. *Am J Surg* 2005;190(3):467–473.
73. Moore HB, Juarez-Colunga E, Bronsert M et al: Effect of pregnancy on adverse outcomes after general surgery. *JAMA Surg* 2015;150(7):637–643.
74. Salminen P, Tuominen R, Pajanen H et al: Five-year follow-up of antibiotic therapy for uncomplicated acute appendicitis in the APPAC randomized clinical trial. *JAMA* 2018;320:1259–1265.
75. Yang J, Wen SW, Krewski D et al: Association of treatments for acute appendicitis with pregnancy outcomes in the United States from 2000 to 2016: Results from a multi-level analysis. *PLoS One* 2021;16(12):e0260991.
76. Harju J, Juvonen P, Kokki H et al: Minilaparotomy cholecystectomy with ultrasonic dissection versus conventional laparoscopic cholecystectomy: A randomized multicenter study. *Scand J Gastroenterol* 2013;48:1317–1323.
77. Sjövall S, Kokki M, Kokki H: Laparoscopic surgery: A narrative review of pharmacotherapy in pain management. *Drugs* 2015;75(16):1867–1889.
78. Pearl J, Price R, Richardson W et al: Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. *Surg Endosc* 2011;25:3479–3492.
79. Walsh CA, Tang T, Walsh SR: Laparoscopic versus open appendectomy in pregnancy: A systematic review. *Int J Surg* 2008;6:339–344.
80. Chakraborty J, Kong JC, Su WK et al: Safety of laparoscopic appendectomy during pregnancy: A systematic review and meta-analysis. *ANZ J Surg* 2019;89:1373–1378.
81. Jevtovic-Todorovic V, Hartman RE, Izumi Y et al: Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *J Neurosci* 2003;23:876–882.