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Review

Pregnancy outcome following non-obstetric surgical intervention

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Abstract

Objective: To evaluate the effects of non-obstetric surgical procedures on maternal and fetal outcome.
Methods: A systematic review of all English language literature.
Results: Fifty-four papers met the inclusion criteria. The overall number of patients reported was 12,452. Reported maternal death was rare at .006%. The miscarriage rate was 5.8%; however, this number is difficult to interpret since matched controls were not available. The rate of elective termination of pregnancy following non-obstetric surgery was 1.3%. The rate of premature labor induced by non-obstetric surgical intervention was 3.5% and this was noted specifically following appendectomy versus other types of interventions ($P < .001$). A total of 2.5% of pregnancies resulted in fetal loss. The prematurity rate was 8.2%. The rate of major birth defects among women who underwent non-obstetric surgical intervention in the first trimester was 3.9%. Sub-analysis of papers reporting on appendectomy during pregnancy revealed a high rate (4.6%) of surgery-induced labor. Fetal loss associated with appendectomy was 2.6%; however, this rate was increased when peritonitis was present (10.9%).
Conclusions: Modern surgical and anesthesia techniques appear to diminish the rate of maternal death. Surgery in the first trimester does not appear to increase major birth defects and should not be delayed when indicated. Acute appendicitis with peritonitis is associated with higher risk to the mother and fetus.

Keywords: Pregnancy; Surgery; Pregnancy outcome; Fetus

We systematically reviewed the English literature to determine the effect of non-obstetrical surgical procedures on pregnancy outcome. While more than 8000 urgent surgical procedures are performed each year in pregnant patients [1], the fetal risks have not been critically evaluated. Our goal is to provide the surgeons up-to-date accurate information for decision making in such cases.

Methods

Data sources

A literature search was performed using MEDLINE and Cochrane Controlled Trials Register databases for the years 1966–2002. All of the titles of papers on non-obstetric surgical intervention during pregnancy were considered. Combination of Medical Subject Headings (MeSH) terms (*pregnancy outcome, pregnancy complications, and surgical procedures*) in an "explode" mode was used as search strategy. MeSH terms specific for different non-obstetrical surgical procedures (*appendectomy, cholecystectomy, and laparoscopy*) combined with pregnancy were also used. All titles and abstracts published in the English literature were evaluated, excluding animal studies, comments, letters, editorials, and reviews. References from the retrieved articles and those that were rejected were scanned as well in order to identify further papers.

Study selection

Each article was evaluated according to the preset inclusion criteria. These included studies reporting any surgical intervention, urgent or elective, under anesthesia (regional

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or general) during pregnancy, performed at any trimester of pregnancy, and reporting pregnancy outcome measurements. All types of study design were considered, although studies had to report a series of at least 10 patients to be included. Studies reporting minor interventions or obstetric procedures (eg, skin excisions, chorionic villi sampling, amniocentesis) under local anesthesia during pregnancy were excluded. Papers discussing procedures such as cesarean delivery, fetal surgery, and dilation and curettage were excluded as well. Studies reporting women exposed to known teratogens (eg, chemotherapy or radiotherapy for malignancy) were excluded. Among papers that reported on the same group of patients, only the most recent and updated one was considered to prevent duplication of data.

Data gathering

The quality of the papers was evaluated with respect to study design, number of patients, and whether confounders affecting pregnancy outcome were considered. Data regarding the underlying condition and the indication for the surgical procedure were collected. Pregnancy outcome measurements such as miscarriage, voluntary termination due to surgical intervention in pregnancy, cesaean delivery, or delivery induced by the preceding surgery were retrieved as well. Fetal and newborn outcome such as fetal loss, prematurity, malformations, and post-delivery complication were recorded. Maternal complications following surgical intervention and underlying condition were also collected.

Data analysis

Data were collected and tallied in tabular form. We found high variability among studies in terms of indication for surgery, surgical approach, different anesthetic methods, and improved care for the neonate in the recent years. Meta-analysis was judged to be inappropriate. Therefore, critical synthesis of reasonably similar studies was performed.

Results

The literature search resulted in 4052 titles that were scanned for relevance according to the preset inclusion criteria. Fifty-four articles matched our inclusion criteria and were included in the systematic review; 52 were retrospective cohorts or case series, 1 was a prospective cohort, and 1 described a case-control study (Table 1). Four publications were based on patients' registry data. Thirty-five (65%) publications were published since 1990. Most of the publications focused on acute abdominal conditions requiring urgent or semi-urgent surgical intervention (eg, appendicitis). Only 1 paper focused on thyroidectomy during pregnancy, mainly for malignancy, where decision making could be made electively. Table 2 delineates the studies according to the surgical procedure. In most of the papers, pregnancy outcome was a secondary end point. The focus of most papers was on the surgical aspects of diagnosis and measures associated with the underlying acute medical conditions that required urgent surgical intervention during pregnancy.

Reported patients

The overall number of patients reported in articles based on patients' registries was 12,452; however, overlap of patients was noted in papers originating in the Swedish Registry [2–4]; therefore, each was addressed individually to avoid data duplication. The total number of patients reported excluding the Swedish Registry was 4473 (this number includes 2565 patients reported from the Manitoba Health Insurance records [5].

Fifteen papers did not report the trimester of pregnancy when the surgical intervention took place. The total number of patients reported by trimesters was 1387: 411 patients in the first trimester, 688 in the second, and 288 patients in the third trimester.

Maternal death

Maternal complications following surgical procedure during pregnancy were not reported consistently among the reviewed studies. Only 1 maternal death of a woman undergoing laparoscopic cholecystectomy due to intra-abdominal hemorrhage 2 weeks postoperatively during the 20th week of pregnancy was reported [6]. This corresponds to a maternal death rate of .006%.

Miscarriages

The overall number of reported miscarriages was 236, which is 5.8% of all reported patients who underwent a surgical intervention throughout their pregnancy. In papers that specified trimester of pregnancy, the rate of miscarriages was 10.5% (n = 43) of the pregnant women who were exposed to surgical intervention in the first trimester. Although the rate of miscarriages according to the reviewed papers was not high, it would be very difficult to evaluate this value in the lack of a control group collected in a similar manner but without surgery. The reported patients were exposed to the surgical procedures at various points in their gestational ages, and thus their chances for a naturally occurring abortion, not associated with surgery, would be highly variable as well. Therefore those rates should not be over-interpreted.

Elective termination

From the studies reporting on elective termination following a surgical procedure, 1.3% (n = 23) of women

Table 1
Characteristics of the included publications with the retrieved data

First author and year of publication	Procedure	Study design	N (trimesters: 1,2,3)	Pregnancy outcome			Fetal outcome			Maternal mortality
				SA	TA	Surgery induced delivery	Death	Prematurity	MM	
Finch 1974 [17]	Appendectomy	Retro. series	56 (16,25,15)	0	0	0	4	2	0	0
Mohammed 1975 [18]	Appendectomy	Retro. series	20 (12,6,2)	2	0	0	1	2	0	0
Cunningham 1975 [19]	Appendectomy	Retro. series	34 (10,16,8)	2	0	NA	1	3	0	0
Townsend 1976 [31]	Appendectomy	Retro. series	29 (8,14,7)	1	1	1	2	2	0	0
Gomez 1979 [32]	Appendectomy	Retro. series	35 (9,17,9)	NA	NA	1	0	3	0	0
Punnonen 1979 [33]	Appendectomy	Retro. series	24 (2,14,8)	0	0	2	1	1	0	0
Frisenda 1979 [34]	Appendectomy	Retro. series	37 (10,16,11)	1	0	0	0	1	0	0
Farquharson 1980 [20]	Appendectomy	Retro. series	25 (9,13,3)	NA	NA	1	1	4	0	0
McComb 1980 [35]	Appendectomy	Retro. series	19 (3,9,7)	1	NA	NA	1	3	0	0
Horowitz 1985* [21]	Appendectomy	Retro. series	10 (1,9,0)	1	0	1	3	1	0	0
Doberneck 1985 [36]	Appendectomy	Retro. series	29 (9,14,6)	0	2	3	0	3	0	0
Bailey 1986 [22]	Appendectomy	Retro. series	41 (NA)	1	NA	NA	1	0	1	0
Liang 1989 [23]	Appendectomy	Retro. series	24 (6,12,6)	0	0	3	0	5	0	0
Tamir 1990† [24]	Appendectomy	Retro. series	77 (27,37,13)	2	7	4	0	23	0	0
Mazze 1991 [3]	Appendectomy	Retro. registry	778 (272,400,106)	NA	NA	39	14	57	18	NA
Halvorsen 1992‡ [37]	Appendectomy	Retro. series	12 (0,6,6)	0	0	0	1	2	0	0
To 1995§ [38]	Appendectomy	Retro. series	34 (13,13,8)	5	0	4	0	5	0	0
Al-Mulhim 1996 [25]	Appendectomy	Retro. series	49 (10,31,8)	3	0	7	7	3	0	0
Andersen 1999 [39]	Appendectomy	Retro. series	56 (12,28,16)	4	0	2	1	4	0	0
Hee 1999¶ [26]	Appendectomy	Retro. series	117 (28,67,22)	4	2	0	NA	2	NA	0
Mourad 2000 [27]	Appendectomy	Retro. series	67 (17,27,23)	0	0	1	0	3	0	0
Tracey 2000 [28]	Appendectomy	Retro. series	22 (5,6,11)	0	0	1	0	5	0	0
Sakhri 2001 [29]	Appendectomy	Retro. series	23 (2,6,15)	0	0	0	1	3	0	0
Hsu 2001 [30]	Appendectomy	Retro. series	35 (1,19,5)	0	3	3	1	0	0	0
Hill 1975 [40]	Cholecystect.	Retro. series	20 (NA)	1	1	0	1	0	0	0
Dixon 1987 [41]	Cholecystect.	Retro. series	18 (3,14,1)	0	2	0	0	1	0	0
Swisher 1994 [42]	Cholecystect.	Retro. series	16 (5,11,0)	0	0	0	0	2	0	0
Davis 1995 [43]	Cholecystect.	Retro. series	19 (4,10,5)	0	0	0	0	5	0	0
Steinbroook 1996 [44]	Cholecystect.	Retro. series	10 (NA)	0	0	0	0	0	0	0
Barone 1999 [6]	Cholecystect.	Retro. series	46 (NA)	0	0	1	2	1	1	1
Cosenza 1999 [45]	Cholecystect.	Retro. series	32 (8,22,2)	1	2	0	1	1	0	0
Daradkeh 1999 [46]	Cholecystect.	Retro. series	16 (2,10,4)	0	0	0	0	0	0	0
Muench 2001 [47]	Cholecystect.	Retro. series	14 (NA)	0	0	0	0	1	0	0
Curet 1996 [8]	Laparoscopy	Case control	34 (15,19,0)	0	0	0	0	0	0	0
Amos 1996 [48]	Laparoscopy	Retro. series	12 (NA)	2	0	0	4	0	0	0
Reedy 1997 [4]	Laparoscopy	Retro. registry	3,704 (NA)	NA	NA	NA	30	NA	173	NA
Conron 1998 [9]	Laparoscopy	Retro. series	21 (12,0,9)	1	0	0	1	1	0	0
Akira 1999 [10]	Laparoscopy	Retro. series	35 (NA)	1	0	NA	1	0	0	0
Andreoli 1999 [11]	Laparoscopy	Retro. series	18 (4,11,3)	0	0	0	0	1	0	0
Affleck 1999 [12]	Laparoscopy	Retro. series	98 (NA)	0	0	NA	0	11	0	0
Lyass 2001 [13]	Laparoscopy	Pros. cohort	22 (7,8,7)	0	0	0	0	0	0	0
Rojansky 2002 [14]	Laparoscopy	Retro. series	37 (NA)	2	1	0	0	3	2	0
Hess 1988 [49]	Adnexal	Retro. series	54 (9,41,4)	5	1	0	0	3	0	0
Platek 1995 [50]	Adnexal	Retro. series	19 (NA)	1	0	0	0	0	0	0
Soriano 1999 [51]	Adnexal	Retro. series	93 (64,29,0)	7	NA	0	0	8	3	0
Moore 1999 [52]	Adnexal	Retro. series	14 (0,9,0)	0	0	0	1	3	0	0
Usui 2000 [53]	Adnexal	Retro. series	60 (NA)	2	0	0	3	7	2	0
Hamilton 1968 [54]	Thyroidectomy	Retro. series	24 (5,18,1)	0	0	0	0	1	0	0
Duncan 1986 [5]	Various	Retro. registry	2565 (NA)	181	NA	NA	NA	NA	82	NA
Mazze 1989 [2]	Various	Retro. registry	5405 (2252,1881,1272)	NA	NA	NA	99	423	102	NA
Kort 1993 [55]	Various	Retro. series	78 (0,36,42)	NA	0	NA	3	17	0	0
El-Amin 1998 [56]	Various	Retro. series	41 (NA)	2	0	NA	0	5	0	0
Gerstenfeld 2000 [57]	Various	Retro. series	106 (53,52,1)	2	NA	1	2	11	NA	0
Visser 2001 [58]	Various	Retro. series	76 (NA)	NA	1	4	0	12	1	0

MM = major malformations; NA = not available (information is missing or not clear); Pros = prospective; Retro = retrospective.

* Horowitz et al reported on 12 patients; however, 2 patients were operated on at the puerperium.

† The study by Tamir reported on 84 patients; however, only 77 were eligible for pregnancy outcome analysis; 7 patients were diagnosed at the puerperium.

‡ Halvorsen et al reported on a group of 16 patients; however, the report considers only those who were diagnosed with acute appendicitis.

§ To et al reported on a group of 38 patients; however, 4 patients were treated in the postpartum period, and therefore only 34 were considered for analysis.

¶ Missing data on several patients; information on preterm termination is not available for 5 of 11 patients.

Table 2
The included publications (N = 54) according to the surgical procedure at focus

Surgical procedure	No. of publications
Appendectomy*	24
Cholecystectomy*	9
Laparoscopy†	9
Adnexal mass	5
Miscellaneous	7

* Papers that were focusing on 1 type of condition managed either by laparotomy or laparoscopy.

† Papers discussing laparoscopic procedures focusing on more than 1 type of intervention (eg, laparoscopic appendectomy and laparoscopic cholecystectomy).

elected to terminate. The rationale for termination was not specified in most papers.

Delivery induced by surgical procedure

The rate of delivery induced by the surgical intervention, whether the etiology for that was the procedure itself or the underlying condition was 3.5% (79/2282). This adverse outcome was prevalent in studies reporting on appendectomy in pregnancy. Fewer cases dealing with medical conditions other then appendicitis reported on surgery-induced labor (73/1559 vs. 6/723, $P < .001$).

Fetal outcome

Fetal death

A total of 2.5% (n = 45) of pregnancies resulted in fetal loss. This number does not include studies based on patients' registries. A total of 1.8% (n = 99) of deaths of 5405 cases were reported by the Swedish registry [2]. Later, the same group reported 14 cases of fetal death among 778 (1.8%) patients from the Swedish Registry undergoing appendectomy during pregnancy [3]. Obviously, based on the same database, an overlap exists between the 2 populations. Reedy, based on the Swedish registry as well, reported a rate of .8% (30/3704) of fetal death cases [4].

Table 3
Pregnancy outcome measures for studies reporting on appendectomy during pregnancy

Outcome measure	n	N	%
Miscarriages	27	815	3.0
Elective termination	15	755	2.0
Surgery induced delivery	73	1559	4.7
Fetal loss	40	1536	2.6
Fetal loss in patients with perforated appendix	18	182	10.9
Prematurity	137	1653	8.3
Major birth defects	18	464*	3.9

* Only for patients who were operated on during the first trimester.

Prematurity

The prematurity rate in the reviewed articles was 8.2% (597/7313). This rate includes patients from registries.

Major birth defects

The rate of major birth defects concluded from the reviewed studies was 2.0% (194/9878). The calculation was based on all studies, excluding late reviews of the Swedish Registry [3,4] to avoid data overlap. From studies that reported on patients per trimester and major birth defects, the rate of major malformation among patients who underwent a surgical procedure during the first trimester was 3.9% (105/2663).

Appendectomy in pregnancy

Since appendicitis is more of a homogenous surgical condition, we conducted a sub-analysis of the previous parameters with respect to appendectomy. All papers were retrospective series except for 1 paper based on the Swedish Registry [3]. None of these papers addressed confounders (Table 1).

Data summary for parameters on outcome following appendectomy are presented in Table 3. A unique feature of appendectomy is an apparently high rate of surgery-induced delivery (4.6% or 73/1559). There appears to be a difference between the rate of surgery-induced labor when appendicitis is compared to other medical conditions (73/1559 vs. 6/723, $P < .001$). The fetal loss rate for appendectomy during pregnancy was 2.6% (40/1559) versus 1.2% (56/4485) for other surgical procedures during pregnancy ($P < .001$). The fetal loss rate was 10.9% when peritonitis was present.

Comments

The need for non-obstetric surgery in pregnancy has been estimated to be .12% [1]. This translates to 8000 cases in the United States every year. Estimation of the effect that general anesthesia and surgical intervention have on reproductive risk among these patients is critical in evaluating therapeutic choices.

The available world literature includes more than 10,000 patients in 54 studies. The main focus of these articles was not maternal and fetal outcome but mainly diagnosis, surgical management, or the effects of anesthesia. The wide variability of surgical indication and anesthetic technique and article focus made the comparison and combination of these articles difficult. There was also very little information on other possible confounders of pregnancy outcome such as maternal age, lifestyle, underlying condition, and drugs. For these reasons we felt that meta-analysis of the articles would not be meaningful. Yet, systematic review of these papers does allow several observations:

Maternal outcomes

There was inconsistent reporting of maternal outcomes in the papers. The report of 1 death in approximately 12,542 procedures (.006%) implies that the risk of death is extremely low. This rate is lower than one would expect based on traditional teaching. However, it is possible given the nature of the published papers that some bias against reporting deaths occurred. It seems that concerns over possible maternal death due to anesthesia and surgery alone are not a reason to delay prompt treatment of the underlying surgical condition.

Miscarriage is a big concern for both patient and physician. The overall rate of 5.8% for miscarriage/fetal death for all trimesters and the rate of 10.5% for first trimester patients certainly is concerning. However, the lack of control groups for the patients makes these results difficult to interpret. One cannot separate the contribution of surgery and anesthesia from the underlying medical condition.

Elective termination occurred in 1.3% of women. The reasons for termination of pregnancy were not given. One could speculate that it may be due to fears about possible teratogenicity of anesthetics or concerns over fetal hypoxia. We did note that there appears to be a trend in reporting increased rates of elective termination since 1990. It is not readily apparent why this may be the case. Possible reasons would include improved reporting of outcomes, changes in societal attitudes, or even legal code changes.

The rate of premature delivery induced by the surgical intervention or underlying condition was 3.5% and was only reported in cases of appendectomy. This will be discussed further under the appendectomy section.

Fetal outcomes

The fetal loss rate was 2.5% in non-registry studies and ranged from .8% to 1.8% in registry studies. Interpretation is limited by the lack of a suitable control groups. Premature birth occurred in 8.2% of cases. Improvements in neonatal care have occurred with time and it makes comparison of results across years impossible. Premature labor that might have resulted in fetal loss in 1985 may not have the same outcome today. We noted that the fetal loss rate in studies on appendectomy appeared higher.

The rate of major birth defects in the studies reviewed was 2.0%, excluding late reviews of the Swedish registry data. The rate of major birth defects in patients undergoing surgery during the first trimester was 3.9%. This rate is slightly higher than the expected rate of 1% to 3% for major birth defects in the general population [7]. None of the individual studies showed that the increased rate of birth defects was statistically significant.

Laparoscopic versus open procedures

We identified 9 studies that focused on laparoscopic surgery during pregnancy. None of the studies came to the conclusion that laparoscopic procedures were harmful to the mother or fetus. In general, the most common conclusion was that laparoscopic surgery was safe and may benefit with the patient when compared to open procedures [8–14].

Appendectomy in pregnancy

Appendectomy is probably the most frequently performed non-obstetrical surgical procedure in pregnancy [15,16]. We noted differences in the data for this medical condition when compared to others.

The rate of premature delivery for patients with appendicitis was statistically higher when compared to other medical conditions ($P < .001$). Including registry data, the fetal loss rate for patients undergoing appendectomy was significantly greater than the fetal loss rate ($P < .001$) for patients undergoing other surgical procedures during pregnancy. The already high fetal loss rate during appendicitis increases to 10.9% when peritonitis is present. It appears from these simple comparisons that the effects of acute appendicitis and surgery on the patient are more severe and different from other acute conditions requiring surgery during pregnancy. Most papers on appendectomy concluded that there is worse maternal and fetal outcome if peritonitis develops and encouraged prompt diagnosis and treatment of this condition [17–30].

Summary

We identified 54 papers that provided maternal and fetal outcome data for review. Although maternal death is rare (<1/10,000), it can occur. There appears to be no difference between open and laparoscopic procedures. Premature labor and fetal loss are the most common undesired consequences, especially if acute appendicitis is present. Acute appendicitis has significantly more severe effects on the maternal and fetal outcome particularly if peritonitis develops when compared to other acute surgical conditions during pregnancy.

Based on our review of the literature, we came to the following conclusions:

- Using modern surgical and anesthetic techniques, the risk of maternal death appears to be very low.
- Surgery and general anesthesia do not appear to be major risk factors for spontaneous abortion.
- The rate of elective termination appears to be in the range of the general population.

- Non-obstetric surgical procedures do not increase the risk for major birth defects. Hence, urgent surgical procedures should be performed when needed.
- Acute appendicitis, especially when accompanied by peritonitis, appears to be genuine risk for surgery-induced labor or fetal loss.

This review and analysis underscores our lack of knowledge in this area and points out a critical need for better data, with details not only on surgical condition, the anesthetic and surgical techniques, but also careful attention to confounders such as the underlying maternal condition and its management, smoking, alcohol consumption, socioeconomic status, and many others.

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