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Methods: Systematic review conducted in MEDLINE® Cochrane, EMBASE and LILACS database up to February 16th, 2020. Articles were selected according to study type, type of intervention and outcomes. Articles were selected by more than one researcher based on title, abstract and full text. The SIGN checklist was used for bias assessment.

Results: A total of 55 articles were retrieved from MEDLINE® via Pubmed, Cochrane, LILACS and EMBASE. Sixteen studies were elected for full text reading, and fifteen of them were selected for the concluding paper evaluation.

Conclusion: Articles revealed higher efficacy in the laparoscopic appendectomy when compared to conventional open appendectomy in all trimesters.

Keywords: acute appendectomy during pregnancy; laparoscopic appendectomy; open appendectomy.

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Priscila Scalabrin Longo [α], Ansara Alcantara Durante [σ], Felipe Placco Araujo Glina [ρ], Karina Scalabrin Longo [ω] & Diego Ferreira de Andrade Garcia [¥]

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I. Introduction

Acute appendicitis is the most frequent medical condition that requires surgical intervention during pregnancy. The incidence of acute appendicitis during pregnancy rages from 1.8 to 41 per 10 000 pregnancies, specially during the second trimester.

Pregnancy brings its own difficulties to the surgeon and to the anaesthesiologist, since the normal physiology of the body becomes altered[1].

The history, physical examination and laboratory results are essential for the accurate diagnosis of acute appendicitis. The best signs include pain that starts in the right lower quadrant or that irradiates from peri umbilical to the right lower quadrant. Besides the fact that the patient can be nauseated, misinterpreting the clinic with pregnancy emesis. The Alvarado Score, which includes the criteria migration of pain, anorexia, nausea, tenderness in right lower quadrant, rebound pain, elevated temperature, leucocytosis and shift of white blood cell count to the left, stratifies patients according to their diagnosis and risks[2].

According to the paper Appendectomy: Diagnostic Criteria and Hospital Performance from E. J. Thomas and C. Barber Mueller, appendicitis that is untreated or belatedly treated carries a high mortality risk. Therefore the appendectomy is an attempt to intervene in the progression of obstruction, infection, perforation, peritonitis, and death of patients. The mortality rate in the study varied between 1: 850 and 1: 2300 cases with acute appendicitis.

Although antibiotic treatment has proven to be effective in treating select patients with acute appendicitis, appendectomies remain the standard treatment of choice[3].

Several controversies about the ideal procedure are reported in the medical literature. Despite the significant number of articles that consider both the laparoscopic and open appendectomy as safe procedures, there is no consensus on the optimal surgical management of acute appendicitis in pregnancy nowadays[4].

The safety of the laparoscopic approach for pregnant women has been widely discussed in the past ten years. Most of those studies were single institution researches or with limited number of patients. Some provided low-grade evidence that laparoscopic approach in pregnant women might be associated with a greater risk of fetal loss, of preterm delivery and technical difficulties in the laparoscopic appendectomy[5].

This study was designed to identify surgical and obstetrical outcomes of Laparoscopic Appendectomy (LA) and conventional Open Appendectomy (OA) in pregnant patients with acute appendicitis during all trimesters.

II. Methods

a) Inclusion and exclusion criteria

Selected articles were randomised clinical trials published in English, Portuguese or Spanish, which comprehended pregnant women with acute appendicitis. Interventions consisted on laparoscopic appendectomy and were compared to conventional open appendectomy. Surgical and obstetrical outcomes were included, such as hospital stay, medical expenditure, operation time, gestational age, Apgar scores, birth weight and height, delivery type, time to first flatus, time to oral intake, return to daily activities, need of post operative analgesics, occurrence of

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negative appendectomies, maternal and neonatal morbidity and mortality. Different outcomes were excluded, such as unusual preoperative and postoperative complications, and insignificant obstetric outcomes.

b) Databases

Articles were retrieved from Medline via Pubmed, Cochrane, Lilacs and Embase search until/on February 16th, 2020. The following search strategy was used: ''(acute appendicitis AND pregnancy AND laparoscopic appendectomy AND open appendectomy)''.

c) Selection

Selection process

Eligibility assessment was performed independently by two reviewers (PSL and AAD), in a non-blinded standardised fashion. Disagreements between reviewers were resolved by consensus. Studies were considered at each stage (title, abstract and full text) of the process for the sake of better selection. Study authors were not contacted.

Checklist

The Scottish Intercollegiate Guidelines Network (SIGN)[6] checklist was used to evaluate clinical trials.

d) Critical evaluation

Biases

Selection, performance, detection, mis-understanding and reporting were considered biases.

To ascertain the validity of eligible clinical trials, independent and reliable peer reviewers were selected. They determined the adequacy of allocation concealment and blinding of patients, health care providers, data collectors and outcome assessors. All items above were contemplated in the SIGN[6] evaluation questionnaire.

Extraction results

Results were selected from all articles evaluating surgical and obstetrical outcomes, such as hospital stay, medical expenditure, operation time, gestational age, Apgar scores, birth weight and height, delivery type, time to first flatus, time to oral intake, return to daily activities, need of post operative analgesics, occurrence of negative appendectomies, maternal and neonatal morbidity and mortality. They were evaluated with mean and standard deviation.

III. Results

a) Study selection

PubMed, Cochrane, Lilacs and Embase database search yield 55 records in Medline and in other index, with no duplicates found. Of these, 36 records were screened after title analyses, 16 full-text articles assessed for eligibility after abstract analyses and 15 studies included in qualitative synthesis after full-text reading. One article was excluded for not describing clinical articles.

A total of 15 articles were retrieved. There were no textbooks and dissertations. The search and selection strategy employed was displayed in the Prisma[7] flowchart (Figure 1).

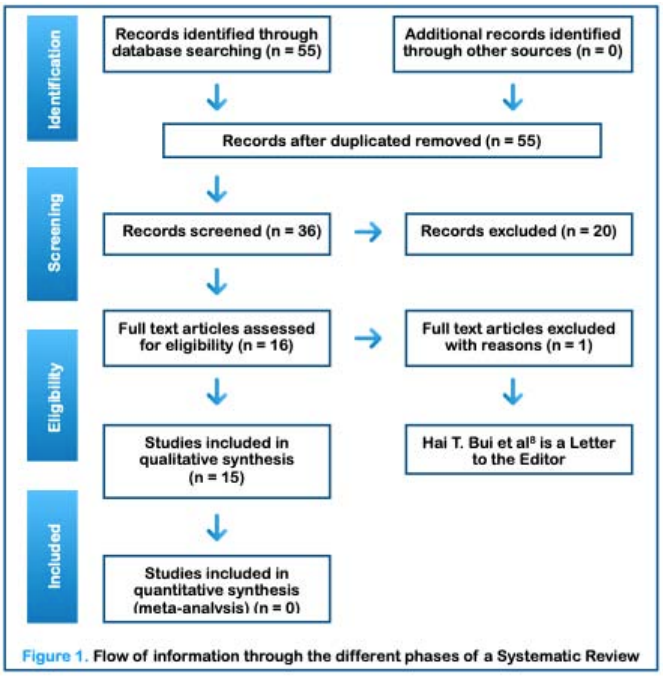


Figure 1. Flow of information through the different phases of a Systematic Review

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Table 1. Study Description

Articles	Study Type	Follow-up (years)	LA (patients)	OA (patients)	Maternal Age	Maternal BMI	Parity	Gestational Age at Delivery	Gestational Trimester at Surgery	Complications Analysed	Phases of Appendicitis
Kwon H et al [9]	RCT	8	35	27	D	D	D	D	1 Tri: 15 LA, 7 OA 2 Tri: 15 LA, 17 OA 3 Tri: 5 LA, 3 OA	Wound Infection, Preterm Labor, Preterm Delivery	ND
Maimaiti A et al [10]	RCT	4	7	19	D	ND	D	ND	1 Tri: 1 LA, 4 OA 2 Tri: 6 LA, 9 OA 3 Tri: 0 LA, 6 OA	Clavein-Dindo Score	AA: 1 LA, 4 OA PA: 5LA, 9 OA CA: 1 LA, 6 OA
Segev L et al [11]	RCT	14	50	42	D	ND	ND	D	Total: 19, OA: Mean 24 weeks LA: Mean 16 weeks	Clavein- Dindo Score	AA: 59 (36 LA, 23 OA) CA: 11 (4 LA, 7 OA)
Laustsen JF et al [12]	RCT	12	19	25	D	ND	ND	ND	1 Tri: 8 LA, 0 OA 2 Tri: 7 LA, 20 OA 3 Tri: 4 LA, 5 OA	Wound Infection, Abscess, Haematoma	AA: 16 (3 LA,13 OA), PA: 20 (13 LA,7 OA), CA: 8 (3 LA, 5 OA)
Karaman E et al [13]	RCT	5	12	36	D	D	D	ND	1 Tri: 1 LA, 2 OA 2 Tri: 7 LA, 12 OA 3 Tri: 4 LA, 22 OA	Wound Infection, Intra-abdominal Abscess	AA: 46 LA/OA PA: 2 LA/OA
Yoo KC et al [14]	RCT	7	24	56	D	D	ND	D	1 Tri: 7 LA, 14 OA 2 Tri: 15 LA, 29 OA 3 Tri: 2 LA, 13 OA	Wound Infection, Intra-abdominal Abscess	AA: 55 LA/OA CA: 11 LA, 14 OA
Aggenbach L et al [15]	RCT	20	7	14	D	ND	D	D	AA: 1 Tri: 3 2 Tri: 7 3 Tri: 6	Clavein- Dindo Score	Normal appendix: 4 Non perforated: 9 Perforated: 3
Cheng HT et al [5]	RCT	5	128	653	D	ND	ND	D	ND	Pre Term Labor, Abortion, Need of Cesarean Section	Not complicated: 544 OA, 116 LA, Complicated: 109 OA, 12 LA
Chung JC et al [16]	RCT	4	22	39	D	D	ND	D	1 Tri: 6 LA, 8 OA 2 Tri: 13 LA, 20 OA 3 Tri: 3 LA, 11 OA	Intra-abdominal Abscess, Wound Infection	ND
Peled Y et al [17]	RCT	9	26	59	D	ND	D	D	ND	Fever > 38^{O}C, Presence of Uterine Contractions	Normal appendix: 5 LA, 10 OA, AA: 19 LA, 37 OA, Perforated: 1 LA, 10 OA
Kapan S et al [18]	RCT	2	10	10	D	ND	ND	ND	ND	ND	ND
Eom JM et al [19]	RCT	10	15	28	D	D	D	D	LA: Median 15 weeks, OA: Median 17 weeks	Pre-Term Deliveries, Uterine Contractions, Abscess, Fever	AA: 11 LA, 22 OA, Gangrenous: 2 LA, 1 OA, Perforated: 2 LA, 5 OA
Kaplan M et al [20]	RCT	3	50	50	D	D	ND	ND	ND	Pain, Wound Infection, Chronic Pain	AA: 95 LA/OA Perforated: 5 LA/OA
Sadot E et al [21]	RCT	9	48	17	D	ND	ND	D	LA: 18.1 ± 7.4 weeks OA: 24.3 ± 6.7 weeks	Wound Infection, Abscess, Postoperative Contractions	G1 Acute: 57% G2 Gangrenous: 3% G3 Perforated: 4,6% G4 Abscess 6%
Kirshtein B et al [22]	RCT	10	23	19	D	ND	ND	D	1 Tri: 23 LA/OA 2 Tri: 19 LA/OA 3 Tri: 0 LA/OA	Wound Infection, Abscess, Urinary/ Pulmonary/ Obstetric Complications	AA: 34 LA/OA CA: 7 LA, 1 OA

RCT: Randomised Clinical Trial; P: Pregnant women; AA: Acute Appendicitis; LA: Laparoscopic Appendectomy; OA: Open Appendectomy; D: Described; ND: Not Described; AA: Acute Appendicitis; PA: Phlegmnous Appendicitis; CA: Complicated Appendicitis

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Table 2. The Scottish Intercollegiate Guidelines Network (SIGN)[6] checklist

Articles for the SIGN Checklist	1.1) The study addresses an appropriate and clearly focused question	1.2) The assignment of subjects to treatment groups is randomised	1.3) Adequate concealment method is used	1.4) Subjects and investigators are kept ''blinded'' to treatment allocation	1.5) Treatment and control groups are similar at the start of the trial	1.6) The only difference between groups is the treatment being investigated	1.7) Relevant outcomes are measured in a standardised, valid and reliable way	1.8) What percentage of individuals or clusters recruited into each treatment arm of the study dropped out before study completion?	1.9) All studies are analysed in groups to which they were randomly allocated (often referred to as intention to treat analysis)	1.10) For studies carried out in more than on site, results are comparable for all sites	2.1) How well was the study performed to minimize bias?
Kwon H et al [9]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Maimaiti A et al [10]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Segev L et al [11]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Laustsen JF et al [12]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Karaman E et al [13]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Yoo KC et al [14]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Aggenbach L et al [15]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE

Cheng HT et al [5]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Chung JC et al [16]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Peled Y et al [17]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Kapan S et al [18]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Eom JM et al [19]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Kaplan M et al [20]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Sadot E et al [21]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE
Kirshtein B et al [22]	YES	YES	CANNOT SAY	CANNOT SAY	YES	YES	YES	NOT DESCRIBED	YES	YES	ACCETABLE

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Table 3. The Survey Summary

Articles	Hospital Stay (days) (OA/LA)	Operation Time (minutes) (OA/LA)	Post Operative Complications (OA/LA) (patients)	Estimated Blood Loss (OA/LA) (cc or mL)	Negative Appende-ctomies (OA/LA) (patients)	Time to First Flatus (OA/LA) (days)	Apgar Score (OA/LA)	Abortion (OA/LA) (patients)
Kwon H et al [9]	7.2 ± 3.0 vs 5.5 ± 3.0, p = 0.03	67.0 ± 31.0 vs 73.5 ± 40.4, p = 0.49	8/27 (29.6%) vs 4/35 (11.5%)	64.8 ± 55.1 vs 64.3 ± 39.4 cc, p = 0.96	X	X	X	X
Maimaiti A et al [10]	6.47 ± 2.72 vs 4.14 ±1.77, p = 0.021	65.21 ± 26.58 vs 42.14 ± 8.63, p = 0.003	Score 7/19 (36,8%) vs 2/7 (28,5%), p = 0.430	12.53 ± 9.95 vs 12.14 ± 8.09 mL	X	2.37 ± 1.11 vs 1.43 ± 0.53, p = 0.009	8.2/10 (82%) vs 8.7/10 (87%), p = 0.53	1/19 (5,2%) vs 0/7 (0%)
Segev L et al [11]	5 vs 3, p < 0.001	60 vs 57, p = 0.8	Score: 10/42 (23,8%) vs 4/50 (8%), p = 0.04	X	11/42 (26,1%) vs 9/50 (18%)	X	9/10 (90%) vs 9/10 (90%), p = 0.7	2/42 (4,7%) vs 2/50 (4%), p = 0.7
Laustsen JF et al [12]	5.5 vs 2.6, p = 0.004	49 vs 69, p = 0.002	9/25 (36%) vs. 1/19 (5.26%), p = 0.03	X	52% vs 16%, p = 0.02	X	8.2/10 (82%) vs 8.7/10 (87%)	X
Karaman E et al [13]	4.28 ± 3.31 vs 3.25 ± 2.45, p = 0.004	38.61 ± 11.5 vs 49.42 ± 11.38, p = 0.007	1/36 (2,7%) vs 0/12 (0%)	X	X	4.0 ± 1.6 vs 2.3 ± 0.3, p = 0.032	8.11 ± 1.62 vs 8.42 ± 1.08, p = 0.552	1/36 (2.7%) vs 1/12 (8.3%), p = 0.34
Yoo KC et al [14]	8.1 (10.4%) vs 5.1 (2.1%), p = 0.044	53.9 (19.2%) vs 52.8 (20.8%), p = 0.815	6/56 (10.7%) vs 4/24 (16.6%), p = 0.477	X	X	2.3 (0.9%) vs 2.0 (1.4%), p = 0.391	X	4/56(7.1%) vs 3/24 (12.5%), p = 0.350

Aggenbach L et al [15]	6.5	60	6/21(28,5%)	X	6/21 (28,5%)	X	X	X
Cheng HT et al [5]	5.5 vs 3.8, p = 0.0005	X	16.7% vs 9.4%, p < 0.05	X	X	X	X	14.34/653 (2,1%) vs 13.88/128 (10,8%)
Chung JC et al [16]	6.9 ± 3.7 vs 4.2 ± 2.9, p = 0.043	47.3 ± 14.7 vs 44.2 ± 16.4, p = 0.48	2/39 (5.1%) vs 1/22 (4.5%), p = 0.76	X	9.8% (10.3% vs 9.1%)	4.0 ± 1.7 vs 2.4 ± 0.4, p = 0.034	9.3 ± 0.2 vs 9.2 ± 0.1, p = 0.70	0/39 (0%) vs 0/22 (0%)
Peled Y et al [17]	3.8 ±1.3 vs 3.7 ± 1.1, p = 0.5	X	15/59 (25.4%) vs 1/26 (3.8%), p = 0.009	X	X	X	8.7 ±1.0 vs 8.9 ± 0.2, p = 0.3	0/59 (0%) vs 1/26 (3.8%), p = 0.3
Kapan S et al [18]	1.1	51.7 vs 56.5	X	X	0/10 (0%) vs 2/10 (20%)	X	X	0/10 (0%) vs 0/10 (0%)
Eom JM et al [19]	5 (3-17) vs 4 (3-7), p = 0.102	55 vs 27.5, p = 0.001	7/28 (25%) vs 1/15 (6.6%), p = 0.224	X	0/28 (0%) vs 0/15 (0%)	X	X	0/28 (0%) vs 0/15 (0%)
Kaplan M et al [20]	75.06 ± 35.14 vs 55.80 ± 20.97 hrs, p < 0.05	49.41 ± 11.76 vs 56.25 ± 10.9, p < 0.05	X	X	7.2%	X	X	X
Sadot E et al [21]	4.2 vs 3.4, p = 0.001	55 ± 25 (17%) vs 54 ± 34 (46%), p = 0.34	X	X	24% (18% vs 27%), p = NS	X	9±0.0 vs 8.91 ± 0.29, p = 0.23	0% (0/16) vs 2,4% (1/41), p = 1.0
Kirshtein B et al [22]	1.4 ± 0.5 vs 2.4 ± 1.7, p = 0.023	28.9 ± 9.2 vs 29.9 ± 6.3, p = NS	0/19 (0%) vs 0/23 (0%)	X	5/19 (26,3%) vs 13/23 (56,5), p = NS	X	8.7/10 (87%) vs 8.9/10 (89%), p = NS	1/19 (5,2%) vs 1/23 (4,3%), p = NS

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b) Study characteristics

All fifteen studies selected for review were randomised controlled trials published in English or Portuguese. Articles can be found in table 1, along with descriptions of sample size, follow-up time, type of access, type of study and patient characteristics.

Risk of bias within studies

Potential study biases are shown in table 2. The SIGN[6] checklist was used to access methodological quality and data reliability in selected studies.

Results of individual studies (the survey summary in Table 3)

Kirshtein B et al[22] from 2009 is a retrospective study from 1997 to 2007 that included 42 pregnant women (mean age 24 years, range of gestation 5-25 weeks), who underwent appendectomy for suspected acute appendicitis (23 LA and 19 OA) in the department at Soroka University Medical Center, Beer Sheva, Israel. Five women with normal preoperative abdominal sonography had acute appendicitis (3 LA, 2 OA). The LA was performed more often by senior surgeons (70% cases) and OA more commonly done by residents (47% cases). Although the length of postoperative hospital stay was slightly prolonged after LA (2.4 days vs 1.4 day), LA was associated in this study as a safe and effective procedure during all trimesters of pregnancy and with good maternal and fetal outcomes.

Sadot E et al[21] from 2009 is a hospital based retrospective review of 65 patients from 1999 to 2008 from the Mount Sinai Hospital and Elmhurst Hospital Center. There were 65 patients (48 LA and 17 OA). The use of LA vs OA significantly increased in the first trimester (100% vs 0%, $p<0.001$) and second trimester (73% vs 27%, $p<0.001$), and OA was used more frequently in the third trimester patients (71% vs 29%, p=NS). Significance was demonstrated in mean length of hospital stay in the LA vs OA group (3.4 days vs 4.2 days, p=0,001). No maternal mortalities occurred. According to the study, while methodological limitations preclude a definite recommendation, laparoscopy appears to be a safe, feasible and efficacious approach for pregnant patients with acute appendicitis in all trimesters.

Kaplan M et al[20] from 2009 is a study of 100 pregnant women who underwent appendectomy (50 LA and 50 OA) at Kirikkale Yuksek Ihtisas Hospital during 2000 and 2003. The patients were randomly assigned to each group and advantages of LA included significantly shorter hospital stay (55.80±20.97 hours vs 75.06±35.14 hours), gastrointestinal quality of life index (85.88±9.73 cases vs 101.30±9.31 cases) and quality of life in the long term (95.14±8.45 cases vs 120.36±10.25 cases). The gastrointestinal quality of life index was developed by Eypasch et al and is not only a measure of the personal perception of the disease but also its emotional, physical and social effects. LA showed to be a safe method in all trimesters, a better quality of life in the early and late period and a shorter hospital stay.

Eom JM et al[19] from 2012 is a retrospective study from 2000 to 2010, with 43 patients analysed (15 LA and 28 OA) in the Kangbuk Samsung Hospital. The LA group, when compared to the OA group, had a hospital stay of 4 days vs 5 days (p=0.102), operating time of 27.5 min vs 55 min (p=0.001), haemoglobin change of 1.0 mg/dL vs 0.8 mg/dL (p=0.269), return to bowel activity of 46 hours vs 38 hours (p=0.362), use of postoperative analgesics of 6.7 cases vs 39.2 cases (p=0.033) and postoperative complications were 6.7% vs 25.0% (p=0.224), such as preterm deliveries, postoperative uterine contractions, intra peritoneal abscess and post-operative fever. The study showed that the LA can be a safe and effective method for treating acute appendicitis during the first and second trimestres of pregnancy. The third trimester remained controversial in this study.

Kapan S et al[18] from 2013 included a retrospective study of 20 patients (10 LA and 10 OA) from 2009 to 2011 in the Emergency Surgery Clinic in the USA. All patients had abdominal pain, 13 had nausea and vomiting associated. Mean Alvarado Score was 7.7 points (7-9), mean leukocyte count was 13920 WBCs per microliter (7200-22300). Mean age of patients was 26 years (19-35), mean gestational age at LA was 17.6 weeks (4-33) and there were 6 patients in the first trimester, 10 patients in the second trimester and 4 patients in the third trimester of pregnancy. This study was inconclusive on choosing one approach and defended that the type of surgery (LA vs OA) depends on the surgeon's experience and preference.

Peled Y et al[17] from 2014 is a retrospective cohort study in a tertiary university affiliated referral medical center from 2000 to 2009. There were 83510 deliveries that occurred during the study period, in which 85 cases (0.10%) with acute appendicitis were eligible for the study (26 LA and 59 OA). There was a significant difference in the mean gestational age at surgery between the 2 groups (14.6 weeks in LA vs 19.3 weeks in OA, p=0.009). Post-operative complications such as fever>38°C or presence of uterine contractions rate was higher in the OA vs LA (25,5% vs 3.8%, p=0.009). In this study LA appeared to be a safe procedure for acute appendicitis during all trimesters of pregnancy, with less post-operative complications compared to open appendectomy.

Chung JC et al[16] from 2013 studied retrospectively 61 patients (22 LA and 39 OA) from 2007 to 2011 at Soonchunhyang University Bucheon Hospital. LA had shorter time to first flatus (2.4±0.4 days vs 4.0±1.7 days, p=0.034), earlier time to oral intake (2.3±1.6 days vs 4.1±1.9 days, p=0.023) and shorter postoperative hospital stay (4.2±2.9 days vs 6.9±3.7 days, p=0.043). In this study LA is contemplated as a

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safe and effective procedure in all trimestres of pregnancy and should be considered the standard treatment alternative to OA.

Cheng HT et al[5] from 2014 was based on the Natural Health Insurance Research Database, from 2005 to 2010. There were 859 pregnant women with acute appendicitis, 653 OA, 128 LA and 78 antibiotics-treatment only. The non-operated group had the highest risk of preterm labor. Risk of abortion following acute appendicitis was antibiotics-only group OR=31.37 (95% CI 13.12-75.01), OA group (OR= 14.34, 95% CI 7.70-26.71) and LA group (OR=13.88, 95% CI 5.50-35.04). This study showed that LA can be performed safely in pregnant patients in all trimesters without bringing additional maternal or foetal complications when compared to the OA group.

Aggenbach L et al[15] from 2015 is a retrospective study, with case reports at the University Medical Center in Groningen, a tertiary care hospital, between 1990 and 2010. There were 21 patients (7 LA, 14 OA) included and 2 cases of maternal morbidity. Premature delivery occurred in 2 out of 6 cases with perforated appendicitis and 2 out of 6 cases following a negative appendectomy. Representative results regarding safety issues and outcome of surgical technique could not be reported based upon their limited study sample size.

Yoo KC et al[14] from 2016 retrospectively revised medical records of pregnant woman who underwent appendectomy between 2008 and 2015 at 6 hospitals affiliated to Hallym University. A total of 80 patients were evaluated (24 LA and 56 OA). Length of hospital stay was shorter in the LA group (5.1 days vs 8.1 days, p=0.044) There was no significant difference in overall obstetric poor outcome, such as preterm delivery (8.3% vs 7.1%, p=1.000) and fetal loss (12.5% vs 7.1%, p=0,350). Furthermore, this study showed that LA can be safely performed during any trimester of pregnancy.

Karaman E et al[13] from 2016 studied two tertiary referral centres of Yuzuncu Yil and Kafkas University in a retrospective study from 2010 to 2015. There were 48 patients (12 LA, 36 OA). The LA group had shorter hospital stay (3.25 ±2.45 days vs 4.28±3.31 days, p=0,004), earlier mobilisation time (8.1±2.2 hours vs 10.1±1.6 hours, p=0.025) and shorter time to first flatus (2.3±0.3 days vs 4.0±1.6 days, p=0,032). The OA had statistically shorter operation time than LA (38.61±11.5 min vs 49.42±11.38 min, p=0,007). This study showed that LA appears to be as safe and effective as OA in pregnant patients during all trimesters, without increasing adverse perinatal outcomes.

Laustsen JF et al[12] from 2016 is a retrospective review of all patients who underwent appendectomy during pregnancy from 2000 to 2012, with 44 patients (19 LA, 25 OA) in Odense University Hospital, Denmark. It was noticed in the LA group longer operation time (69 min vs 49 min, p=0,002), but fewer complications (wound infection, abscess and haematoma), shorter hospital stay (2.6 days vs 5.5 days, p=0,004) and lower rate of negative appendectomies (16% vs 52%, p=0,02). In this study, LA is considered safe for both mother and foetus during pregnancy, not depending on gestational age, and also associated with low risk of post-operative complications.

Segev L et al[11] from 2016 is a large contemporary cohort study, that reviewed all women who underwent appendectomy during pregnancy in a single university-affiliated, tertiary medical center during 2000 to 2014. There were 92 patients who met the criteria, 50 cases (54%) in LA and 42 cases (46%) in OA. The laparoscopic group had lower median gestational age at surgery (16 weeks vs 24 weeks, p<0,001), shorter median hospital stay (5 days vs 3 days, p<0,001) and lower rate of postoperative complications (8% vs 24%, p=0,04). There was no difference at Apgar scores, preterm delivery and fetal loss. This study defends LA as a safe procedure and with better surgical outcomes during pregnancy in all trimesters.

Maimaiti A et al[10] from 2017 compared 26 pregnant women from 2012 to 2016 retrospectively, with 7 patients in LA and 19 in OA group from the First Affiliated Hospital of Xinjiang Medical University. Median gestational period was 21,5 weeks (5-33 weeks) and median age of patients was 28 years (19-39 years). There was significantly shorter operation time (42.14±8.63 min vs 65.21 ±26.58 min, p=0,003), hospital stay (4.14±1.77 day vs 6.47±2.72 day, p=0,021) and earlier recovery of gastrointestinal function in the LA group vs the OA group. This study appoints LA as the preferred approach compared to OA, without increased risks for the foetus or the mother.

Kwon H et al[9] from 2018 is a retrospective study between 2008 and 2016 that included 62 patients, 35 cases (56,5%) in the LA group and 27 cases (43,5%) in the OA group in the Obstetrics and Gynecology Department of Dongguk University Ilsan Hospital, Korea. The study showed that LA had shorter hospital stay (5.5 days vs 7.2 days, p=0,03) and lower pain on postoperative score (4 points vs 2.4 points, p<0,01) than OA. No significant differences in operative and surgical complications were found. In this study LA was considered to be feasible and safe in all trimesters without adverse effects on pregnancy.

IV. Discussion

a) Summary of evidence

The hypothesis that LA would have a better impact on surgical and obstetrical outcomes compared to OA was confirmed by literature data, which offered high quality, robust evidence revealing great improvement in the laparoscopic approach during all trimesters of pregnancy. Only randomised clinical trials were included in this study. Up until now it was believed that LA and OA would have similar rates of surgical and

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obstetrical outcomes. However, the selected studies of this systematic review disclosed otherwise.

Kapan S et al[18] from 2013 said it has been more than a hundred years since Balber stated that ''the mortality of appendicitis complicating pregnancy is the mortality of delay''. Delay in the diagnosis of appendicitis is associated with significant complications. Therefore the pathology must be diagnosed and treated with precision, accuracy and promptitude. According to the paper, acute appendicitis has a challenging diagnosis in the pregnant women and early surgical intervention should be performed with any suspicion.

Sadot E et al[21] from 2009 showed that it is likely not the surgical approach itself but the underlying diagnosis combined with maternal factors that determine the risk for pregnancy complications. One of the benefits of the laparoscopic approach is the diagnostic ability to identify other intra abdominal pathologies which may mimic appendicitis and harbour pregnancy risks.

Kaplan M et al[20] from 2009 also showed that the laparoscopic method has the advantage of being a diagnostic procedure for other pathologies, when negative appendectomy arrives at the surgeon's hands, which is hardly manoeuvred in the open method.

When Eom JM et al[19] from 2012 compared the LA to the OA group, they pointed out the necessity of general anaesthesia, the possibility of incidental injury of the gravid uterus with a veress needle or a trocater, the potential effects of increased intra-abdominal pressure on the uteroplacental circulation, concerns related to the use of CO2 and the technical difficulties found in the end of the third trimester of pregnancy. The study supported the idea that LA could not be performed with a gravid uterus large enough to occupy the entire abdominal cavity, such as in a multifetal pregnancy or during the end of the third trimester.

Cheng HT et al[5] from 2014 exemplifies what many studies evaluated in this paper showed: the laparoscopic approach has several well-known advantages over the open technique, such as a better visualisation of the abdominal cavity, fewer wound infections, less post-operative pain, shorter hospital stay and earlier return to daily activities. They also found that LA had reduced and fewer risks for maternal complications compared to OA, being considered a safe and preferable technique in pregnant women with acute appendicitis in all trimesters of pregnancy.

V. Conclusion

There is evidence to support the hypothesis that laparoscopic appendectomy has less impact on surgical and obstetrical complications as compared to conventional open appendectomy during the whole period of pregnancy. However, more studies ought to be promoted to further support the evidence presented.

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