

REVIEW ARTICLE

Diagnostic Performance of Magnetic Resonance Imaging for Detection of Acute Appendicitis in Pregnant Women; a Systematic Review and Meta-Analysis

Mohsen Motavaselian¹, Fatemeh Bayati², Reza Amani-Beni³, Amirreza Khalaji⁴, Sara Haghverdi⁵, Zeynab Abdollahi⁶, Arash Sarrafzadeh⁷, Amir-masood Rafie Manzelat⁸, Amir Rigi⁹, Razman Arabzadeh Bahri¹⁰, Zahra Nakhaee¹¹, Mahta Fadaei¹², Hajar Ghasemi Falaverjani¹³, Sara Malekpour-Dehkordi¹⁴, Maryam Hoseinpour¹⁴, Matin Bidares¹⁵, Sarvenaz Zandkarimi¹⁶, Rasha Ahmadi¹⁷, Dorsa Beheshtiparvar⁸, Seyyed-Amirabbas Ahadiat¹⁸, Mohsen Farshi⁸, Mehrdad Farrokhi^{19*}

1. School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
2. USERN Office, Kermanshah University of Medical Sciences, Kermanshah, Iran.
3. School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
4. Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
5. Kermanshah University of Medical Sciences, Kermanshah, Iran.
6. Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
7. School of Dentistry, Arak University of Medical Sciences, Arak, Iran.
8. School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
9. Islamic Azad University, Zahedan Branch, Zahedan, Iran.
10. Tehran University of Medical Sciences, Tehran, Iran.
11. Gonabad University, Gonabad, Iran.
12. School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
13. Department of Internal Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
14. Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
15. Islamic Azad University of Najafabad, Najafabad, Iran.
16. Faculty of Pharmacy, Islamic Azad University of Tehran Medical Sciences, Tehran, Iran.
17. Shariati Hospital, Tehran University of Medical Science, Tehran, Iran.
18. Research Center of Biochemistry and Nutrition in Metabolic Disorder, Kashan University of Medical science. Kashan, Iran.
19. Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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Abstract: **Introduction:** The diagnosis of acute appendicitis (AA) in pregnant women is commonly challenging owing to the normal results of laboratory tests, organ displacement, and normal physiological inflammatory alterations. This meta-analysis aimed to investigate the accuracy of magnetic resonance imaging (MRI) in diagnosis of AA in pregnant women. **Methods:** Two investigators independently performed a comprehensive systematic literature search of electronic databases including MEDLINE, Cochrane Central, EMBASE, Web of Science, Scopus, and Google Scholar to identify studies that reported accuracy of MRI for diagnosis of AA in pregnant women from inception to April 1, 2022. **Results:** Our systematic search identified a total of 525 published papers. Finally, a total of 26 papers were included in the meta-analysis. The pooled sensitivity and specificity of MRI in diagnosis of AA in pregnant women were 0.92 (95% CI: 0.88–0.95) and 0.98 (95% CI 0.97–0.98), respectively. The pooled positive likelihood ratio and negative likelihood ratio were 29.52 (95% CI: 21.90–39.81) and 0.10 (95% CI: 0.04–0.25), respectively. The area under hierarchical summary receiver operating characteristic (HSROC) curve indicated that the accuracy of MRI for diagnosis of AA in pregnant women is 99%. **Conclusion:** This meta-analysis showed that MRI has high sensitivity, specificity, and accuracy for diagnosis of AA in pregnant women and can be used as a first-line imaging modality for suspected cases of AA during pregnancy. Furthermore, it should be noted that when the result of ultrasonography is inconclusive, the use of MRI can reduce unnecessary appendectomy in pregnant patients.

Keywords: Appendicitis; magnetic resonance imaging; meta-analysis; pregnancy



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1. Introduction

Acute appendicitis (AA) is known as one of the most prevalent non-obstetric causes of acute abdominal pain requiring surgical intervention during pregnancy (1, 2). However, in pregnant cases, the diagnosis of AA is commonly challenging owing to the normal results of laboratory tests, organ displacement due to the altered anatomy of gravid uterus, and normal physiological inflammatory alterations including increased white blood cell count and left shift of neutrophils. Moreover, there is a broad range of manifestations and differential diagnoses due to other causes of acute abdominal pain in pregnant women (3-5). These challenges can delay the diagnosis of AA and surgery, which increases the rate of appendiceal perforation, morbidity, and mortality of pregnant women and the fetus. On the other hand, false-positive diagnosis can result in unnecessary surgeries, increasing risk of unfavorable outcomes including fetus loss and premature labor. Therefore, prompt and accurate diagnosis of AA during pregnancy is needed to reduce morbidity and mortality among both fetuses and pregnant women (4, 6). Despite recent advances in imaging modalities, there are still a considerable minority of patients in whom the appendix is not confidently detected. Furthermore, while ultrasonography is the first-line recommended diagnostic imaging, the majority of investigations are inconclusive or the appendix is not identified. In this regard, previous investigations have shown that computed tomography (CT) scan may have a better accuracy compared to ultrasonography (7-9).

Furthermore, these investigations have revealed the lower efficacy of ultrasonography in diagnosis of AA in cases whose AA had been already diagnosed using other imaging modalities. The use of CT has been approved for assessment of cases suspected of AA with results showing decreased health-care costs and fewer unnecessary surgical interventions. On the other hand, it should be noted that use of CT scan is accompanied with ionizing radiation, which is worrying during pregnancy (10). Due to availability, not causing radiation, and its better visualization of appendix compared to ultrasonography, magnetic resonance imaging (MRI) is being increasingly recommended as an alternative for assessment of pregnant cases with acute abdominal pain and inconclusive ultrasonography imaging. Several investigations have shown

that MRI has an appropriate diagnostic performance for visualizing appendix during pregnancy (11). However, these studies were conducted in different medical centers and due to the difference in training and experience of MRI readers and also the quality of imaging, there is a wide range of diagnostic accuracy in the literature. Therefore, in this meta-analysis, we aimed to investigate the accuracy of MRI in diagnosis of AA in pregnant women.

2. Methods

This systematic review and meta-analysis was carried out according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.

2.1. Search strategy

Two researchers (MF and RA) independently performed a comprehensive systematic literature search of electronic databases including MEDLINE, Cochrane Central, EMBASE, Web of Science, Scopus, and Google Scholar to identify studies that had reported accuracy of MRI for diagnosis of AA in pregnant women from inception to April 1, 2022. The eligible published papers were found using the following keywords, MeSH terms, and Emtree (Embase subjects heading) terms: acute appendicitis, appendicitis, magnetic resonance, magnetic resonance imaging, MR, MRI, pregnancy, pregnant, gestational period, and right lower quadrant pain. The combination of these search terms was also assessed using the Boolean operators AND and OR.

The search strings used were “((acute appendicitis OR appendicitis OR right lower quadrant pain) AND (magnetic resonance OR magnetic resonance imaging OR MR OR MRI) AND (pregnancy OR pregnant OR gestational period))”.

The structured search was limited to human studies, but without language restriction and was concluded when no further studies could be found. In cases where several versions of a study were identified, the most relevant and recently published study was included in our analysis. The reference list of the eligible studies was reviewed in depth to identify other relevant studies, which were not included via systematic search.

2.2. Eligibility criteria

Diagnostic studies were deemed eligible for inclusion in the present study if they had investigated the accuracy of MRI for diagnosis of AA in pregnant patients and reported the main diagnostic parameters including sensitivity, specificity, true positive (TP), false positive (FP), false negative (FN), and

* **Corresponding Author:** Mehrdad Farrokhi; Men's Health and Reproductive Health Research Center, Shohadaye Tajrish Hospital, Tehran, Iran. Email: dr.mehrdad.farrokhi@gmail.com, Phone number: +989384226664, ORCID: 0000-0002-1559-2323.



true negative (TN). Moreover, the diagnostic gold standard for AA used by the included studies were clinical follow-up and surgical pathology. Conference abstracts, reviews, meta-analyses, cases reports, cases series with less than ten cases, non-reviewed preprints, and studies that had no full text were excluded.

2.3. Study selection

Non-duplicate relevant studies were assessed by title and abstract, and then full-text of potentially eligible studies were reviewed. The eligible studies were screened for inclusion in the meta-analysis by two independent investigators and any disagreements between them were settled through discussion with a third researcher.

2.4. Data extraction and risk of bias evaluation

Two investigators independently extracted data from the included studies using a predesigned abstraction form on Excel. The extracted data from the studies included first author, the year of publication, study country, number of patients, mean age, TP, FP, FN, TN, sensitivity, and specificity of MRI for diagnosis of AA. The risk of bias of the included studies was investigated using Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2.

2.5. Statistical analysis

Statistical analysis was performed using Meta-DiSc software version 1.4 and Comprehensive Meta-Analysis software version 3. Q-statistic and I² were used to assess heterogeneity of the included studies. The pooled sensitivity, specificity, and negative likelihood ratio were investigated using random-effects model. The pooled positive likelihood ratio and diagnostic odds ratio were calculated using fixed-effects model.

The forest plots and summary receiver operating characteristic (SROC) curves were used to investigate sensitivity, specificity, and accuracy of MRI for diagnosis of AA in pregnant women. For the evaluation of publication bias, Egger's and Begg's tests were carried out and funnel plots were assessed. Investigation of publication bias and funnel plot were performed using Stata statistical software package (Stata Corp., College Station, TX, USA) (version 17.0).

3. Results

3.1. Search results

Our systematic search through electronic databases identified a total of 525 published papers. After removing 169 duplicates, the remaining 356 papers were screened based on the title and abstract. During this stage, 285 papers did not meet the inclusion criteria.

71 papers were retrieved and evaluated for eligibility based

on full text. Of these, papers that had not reported diagnostic variables (including sensitivity, specificity, TP, FP, FN, and TN) or those that were not classified original diagnostic studies, such as reviews, meta-analyses, case reports, and cases series, and comments were excluded from the meta-analysis. Finally, a total of 26 papers were included in the qualitative and quantitative synthesis. The PRISMA flowchart of the included studies is shown in figure 1.

3.2. Study Characteristics

The baseline characteristics and diagnostic parameters of the included studies are summarized in table 1. A total of 26 diagnostic studies were included in our study with their sample size ranging from 18 to 709 cases. The included studies were published between 2013 and 2021. Mean age of the studied pregnant women ranged between 25 and 32 years. The majority of the included studies were based in USA. Table 2 depicts the summary of risk of bias for the included studies.

3.3. Diagnostic accuracy of MRI

Spearman rank correlation test revealed that logit of 1-specificity positively correlated with logit of sensitivity ($r=0.05$ and $P=0.80$), indicating that there was no threshold effect in the meta-analysis. The heterogeneity of the results of the included studies was evaluated regarding sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio. The results showed a significant heterogeneity for sensitivity, specificity, and negative likelihood ratio ($I^2 = 63.5\%$, $P<0.01$; $I^2 = 40.9\%$, $P = 0.01$; $I^2 = 88.2\%$, $P<0.01$, respectively). However, there was no significant heterogeneity for positive likelihood ratio and diagnostic odds ratio ($I^2 = 23.2\%$, $P = 0.14$; $I^2 = 4.5\%$, $P = 0.39$). Therefore, fixed effect model was used for analysis of positive likelihood ratio and diagnostic odds ratio. Sensitivity, specificity, and negative likelihood ratio were analyzed using random effect model.

The pooled sensitivity and specificity of MRI in diagnosis of AA in pregnant women were 0.92 (95% CI: 0.88–0.95) and 0.98 (95% CI 0.97–0.98), respectively (Figure 2). The pooled positive likelihood ratio and negative likelihood ratio were 29.52 (95% CI: 21.90–39.81) and 0.10 (95% CI: 0.04–0.25), respectively (Figure2). Moreover, the diagnostic odds ratio of MRI was 373.75 (95% CI: 211.86–659.35) (Figure 2). The area under HSROC curve was 0.99, indicating that the accuracy of MRI for diagnosis of AA in pregnant women is 99% (figure 3).

3.4. Publication Bias

The funnel plot of standard error was assessed using log ORs. Publication bias was not found as the funnel plot was distributed symmetrically. Moreover, Egger's test ($P=0.68$) and Begg's test ($P=0.50$) did not show significant publication bias for log DOR (Figure 4).



4. Discussion

Although many original studies have investigated the efficacy of MRI for diagnosis of AA in pregnant women, there is a lack of high-level evidence such as systematic reviews and meta-analysis regarding accuracy of MRI for diagnosis of AA during pregnancy. Our meta-analysis revealed that sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and SROC of MRI in diagnosis of AA in pregnant women were 0.92, 0.98, 29.52, 0.10, 373.75, and 0.99, respectively. It is commonly known that diagnostic efficacy is low at area under the SROC of 0.50-0.60, medium at 0.70-0.90, and high at greater than 0.90, with a positive likelihood ratio > 10.00 and a negative likelihood ratio < 1.00. Therefore, based on the findings of our meta-analysis, MRI has high diagnostic efficacy for identifying AA in pregnant women.

These findings suggest that considering the possible problems of CT scan during pregnancy, including exposure of pregnant women and their fetus to ionizing radiation, MRI, seems to be a promising alternative to CT scan for diagnosis of AA in pregnant women, especially in medical centers with experienced radiologists. The high diagnostic efficacy of MRI may be explained by excellent soft-tissue contrast and lower effect of large body size or the experience of the technician (12). The origin of heterogeneity among included studies may be attributed to type of MRI center (academic hospital and community hospital), experience of interpreter of images, and type of MRI devices.

In a systematic review by Basaran et al. (13) five published paper related to the use of MRI and three related to the use of CT scan for diagnosis of AA in pregnant women were included. Similar to our meta-analysis, the findings of their included studies were compared with the results of surgical pathology. The overall sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of MRI for diagnosis of AA in suspected pregnant cases were 80%, 99%, 22.7, and 0.29, respectively. They concluded that CT scan and MRI can be used for diagnosis of AA in pregnant cases, especially when the findings of ultrasonography are inconclusive. However, it should be kept in mind that MRI is preferred over CT by practitioners due to the safety of MRI during pregnancy.

In another systematic review and meta-analysis, Duke et al. (11) performed a systematic search in PubMed and EMBASE to find all the studies that used MRI for diagnosis of AA. They included 30 studies with a total of 2665 patients. They reported that the sensitivity and specificity of MRI in diagnosis of AA are 96%. Furthermore, they conducted a subgroup analysis on studies that investigated use of MRI in pregnant patients. The results of subgroup analysis revealed that sensitivity and specificity of MRI in pregnant patients were 94% and 97%, respectively.

The difference between our diagnostic parameters with those reported in the aforementioned studies may in part be clarified by the greater number of included studies in the present meta-analysis.

Although American College of Radiology recommended MRI as modality of choice for diagnosis of AA in pregnant patients, there are some critical issues that can affect the accuracy of this imaging modality (14). A recent investigation by Al-Katib et al. (15) has shown that type of imaging center can affect the accuracy of MRI in diagnosis of AA among pregnant cases. They found that diagnostic quality of MRI is higher in main centers compared to community centers. Moreover, their findings revealed that visualization of appendix by radiologist in good quality MRI is considerably higher than suboptimal MRI. Interestingly, in this study, the only case of appendicitis with non-visualized appendix on MRI belonged to the group of patients with suboptimal quality of MRI.

It is crucial to find the source of abdominal pain during pregnancy, especially if the cause of pain is outside the appendix. Previous studies have shown that ultrasonography is an accurate imaging modality for excluding gynecologic sources of right lower quadrant pain and has become increasingly used due to being non-invasive, inexpensive, safe, easy to use, portable, and widely available (16). However, in tertiary centers providing permanent MRI coverage, ultrasonography can be omitted to provide fast-tracked MRI for diagnosis of AA in suspected pregnant women.

5. Limitations

The majority of limitations of our meta-analysis are due to heterogeneity in design, experience of image reviewers, and reporting of results among the primary published papers. Moreover, it should be noted that the majority of the included studies used pathological evaluation for the approval of appendicitis in cases who underwent surgery, while there are accumulating lines of evidence proposing that AA may resolve after conservative treatments. Another limitation of the included studies was that in some of them, the data were collected from medical records, retrospectively. It is possible that the symptoms of some cases improved and they were discharged, but were later admitted to a different medical center with the same symptoms and underwent surgery with the diagnosis of AA.

6. Conclusion

This meta-analysis showed that MRI has high sensitivity, specificity, and accuracy for diagnosis of AA in pregnant women and can be used as a first-line imaging modality for suspected cases of AA during pregnancy. Furthermore, it should be noted that when the result of ultrasonography is inconclusive, the use of MRI can reduce unnecessary appen-



dectomy in pregnant patients.

7. Declarations

7.1. Acknowledgments

The authors thank all those who contributed to this study.

7.2. Authors' contributions

All authors contributed to study design, data collection, and writing the draft of the study.

7.3. Funding

None.

7.4. Conflict of interest

None.

7.5. Data Availability

Not applicable.

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Table 1: Characteristics of the studies included in meta-analysis

Study	Year	Country	Sample Size	Age (Mean)	TP	FP	FN	TN	Sens	Spec
Ahmed et al. (17)	2021	USA	141	26	9	5	0	127	1	0.96
Badr et al. (18)	2021	Belgium	85	29	6	1	0	78	1	0.987
Lukenaite et al. (19)	2020	Lithuania	37	30.37	5	0	1	32	0.83	1
Aguilera et al. (20)	2018	USA	52	25	2	0	9	41	0.18	1
Kereshi et al. (21)	2018	USA	204	29	14	1	0	189	1	0.99
Wi et al. (22)	2018	South Korea	125	32	24	5	0	96	1	0.95
Burns et al. (12)	2017	Canada	63	31	11	0	2	50	0.85	1
Tsai et al. (23)	2017	USA	223	28.4	13	6	1	198	0.92	0.97
Darshan et al. (24)	2017	Canada	42	25.5	3	3	2	34	0.6	0.92
Abadi et al. (25)	2016	Israel	49	NA	5	1	0	43	1	0.98
Al-Katib et al. (15)	2016	USA	58	28	6	1	0	51	0.86	1
Burke et al. (26)	2015	USA	709	27.5	61	5	2	641	0.97	0.99
Konrad et al. (27)	2015	USA	114	NA	16	2	0	96	1	0.98
Ramalingam et al. (28)	2015	USA	102	26.2	8	6	0	88	1	0.94
Theilen et al. (29)	2015	USA	171	NA	12	6	1	152	0.92	0.96
Fonseca et al. (30)	2014	USA	31	NA	11	0	0	20	1	1
Rapp et al. (31)	2013	USA	212	26	17	6	2	187	0.89	0.97
Jang et al. (32)	2011	South Korea	18	31.7	5	0	0	13	1	1
Masselli et al. (33)	2011	Italy	40	28	5	0	0	35	1	1
Oto et al. (34)	2009	USA	118	24.7	9	2	1	106	0.9	0.98
Pedrosa et al. (35)	2009	USA	148	29	14	2	0	132	1	0.99
Vu et al. (36)	2009	Canada	19	31	1	0	1	17	0.5	1
Israel et al. (37)	2008	USA	33	25.6	4	0	1	28	0.8	1
Pedrosa et al. (38)	2006	USA	51	28.3	4	3	0	44	1	0.94
Bichard et al. (39)	2005	USA	29	25	3	0	0	26	1	1
Cobben et al. (40)	2004	Netherlands	12	28	3	0	0	9	1	1

Sens: sensitivity; Spec: specificity; TP: true positive; FP: false positive; FN: false negative; TN: true negative.



Table 2: Quality assessment of the included studies using QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Ahmed et al.	☺	☺	☺	☺	☺	☺	☺
Badr et al.	☺	☺	☺	☺	☺	☺	☺
Lukenaite et al.	☺	?	?	☺	☺	☺	☺
Aguilera et al.	☺	☺	☺	☺	☺	☺	☺
Kereshi et al.	☺	?	☺	☺	☺	☺	☺
Wi et al.	☺	?	?	☺	☺	☺	☺
Burns et al.	☺	?	?	☺	☺	☺	☺
Tsai et al.	☺	☺	☺	☺	☺	☺	☺
Darshan et al.	☺	☺	☺	☺	☺	☺	☺
Abadi et al.	☺	☺	☺	☺	☺	☺	☺
Al-Katib et al.	☺	☺	☺	☺	☺	☺	☺
Burke et al.	☺	☺	☺	☺	☺	☺	☺
Konrad et al.	☺	☺	☺	☺	☺	☺	☺
Ramalingam et al.	☺	☺	?	?	☺	☺	☺
Theilen et al.	☺	?	☺	☺	☺	☺	☺
Fonseca et al.	☺	☺	?	☺	☺	☺	☺
Rapp et al.	☺	?	☺	☺	☺	☺	☺
Jang et al.	☺	☺	☺	☺	☺	☺	☺
Masselli et al.	?	☺	?	☺	☺	☺	☺
Oto et al.	☺	☺	☺	☺	☺	☺	☺
Pedrosa et al.	☺	☺	☺	☺	☺	☺	☺
Vu et al.	☺	☺	☺	☺	☺	☺	☺
Israel et al.	☺	☺	☺	☺	☺	☺	☺
Pedrosa et al.	☺	☺	☺	☺	☺	☺	☺
Bichard et al.	☺	☺	☺	☺	☺	☺	☺
Cobben et al.	☺	☺	☺	☺	☺	☺	☺

☺: Low Risk; ☹: High Risk; ?: Unclear Risk



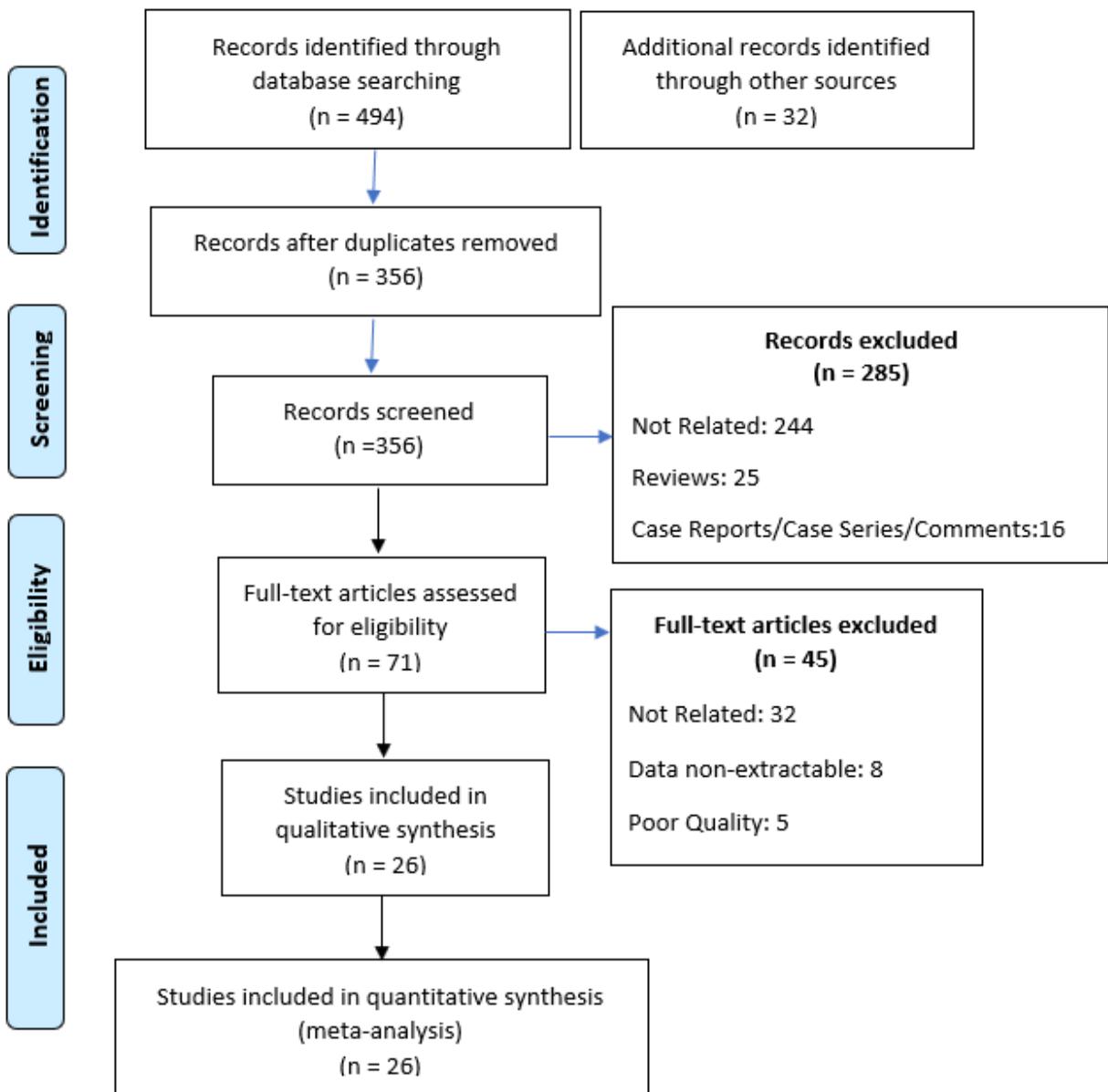


Figure 1: PRISMA flowchart of the literature search and selection of studies that reported accuracy of magnetic resonance imaging (MRI) for diagnosis of acute appendicitis in pregnant women.



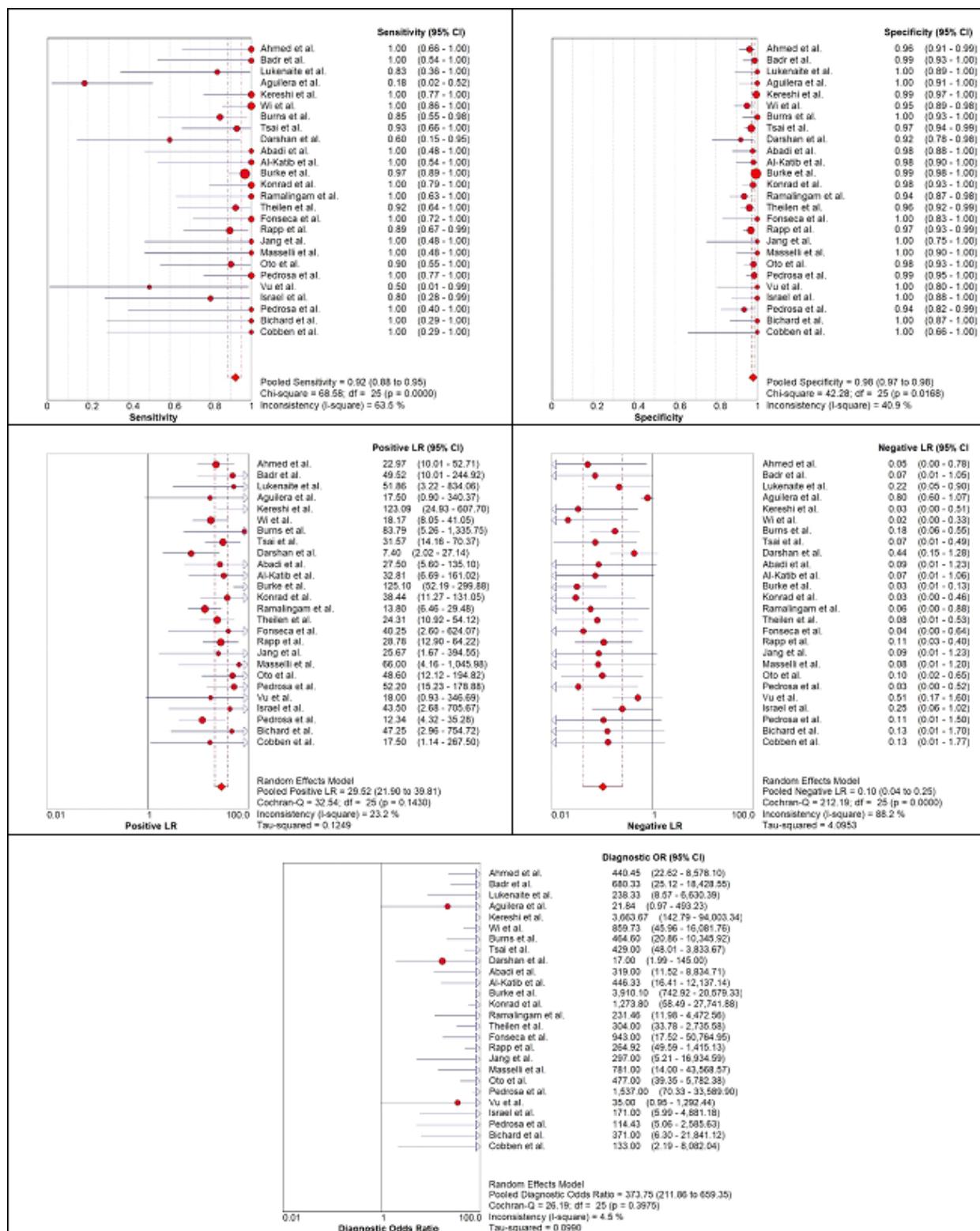


Figure 2: Forest plot of the pooled sensitivity, specificity, positive likelihood ratio (LR), negative LR, and diagnostic odds ratio (OR) of magnetic resonance imaging (MRI) for diagnosis of acute appendicitis in pregnant women. CI: confidence interval.



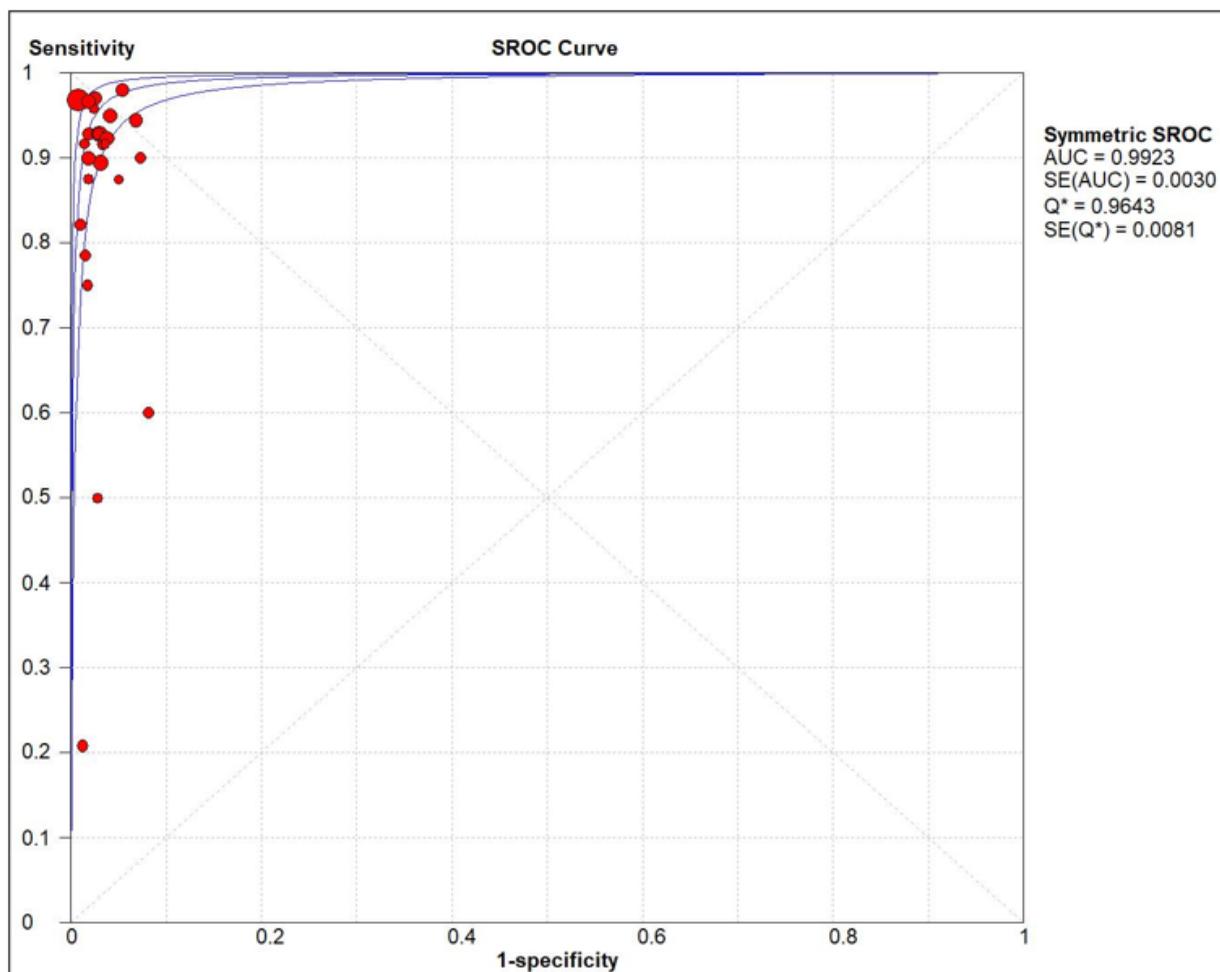


Figure 3: Hierarchical summary receiver-operating characteristic (HSROC) curve indicating accuracy of magnetic resonance imaging (MRI) for diagnosis of acute appendicitis in pregnant women.



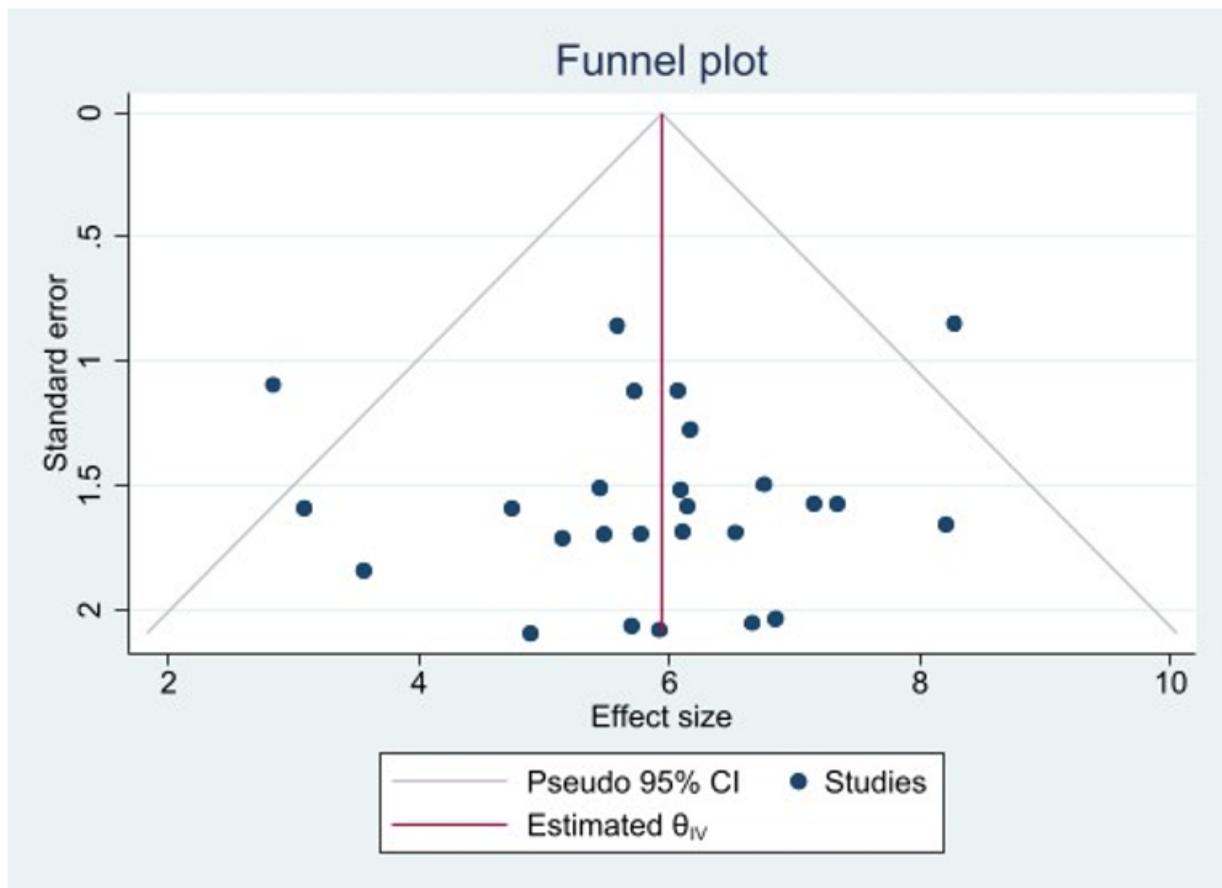


Figure 4: Funnel plot of publication bias for the included studies.