Indian J Med Res 154, September 2021, pp 446-454
DOI: 10.4103/ijmr.IJMR_817_18

Quick Response Code:

Systematic Review

A systematic review on the prevalence of endometriosis in women

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Received April 28, 2018

***Background & objectives*: Endometriosis is one of the causes of female infertility, but the prevalence of endometriosis is not exactly known. We conducted a systematic review and meta-analysis to provide an estimate of the prevalence of endometriosis in women considering the stage of disease, diagnostic method, geographical distribution, clinical symptoms and sample size.**

***Methods*: MEDLINE, Web of Science, Google Scholar, Scopus and Cumulative Index of Nursing and Allied Health were searched to identify peer-reviewed studies published from January 1990 to December 2018 reporting the prevalence of endometriosis. Relevant additional articles were identified from the lists of the retrieved articles. Studies with cross-sectional design were included in the meta-analysis.**

***Results*: The overall prevalence of endometriosis was 18 per cent [95% confidence interval (CI): 16-20] and the prevalence of endometriosis by stage ranged from two per cent (95% CI: 1-4) for stage 4 to 20 per cent (95% CI: 11-28) for stage 1. The prevalence levels of endometriosis in women with infertility, chronic pelvic pain and asymptomatic were 31 (95% CI: 15-48), 42 (95% CI: 25-58) and 23 per cent (95% CI: 19-26), respectively.**

***Interpretation & conclusions*: The results of this study showed that the prevalence of endometriosis in developing countries was high. Future studies are needed to explore other factors affecting the prevalence of endometriosis worldwide, which may help develop future prevention programmes.**

Key words Endometriosis - prevalence - quality assessment - women

Endometriosis affects about 6-10 per cent of women worldwide[1]. In Canada and the United States, the incidence of endometriosis ranges from 5 to 15 per cent in the women of reproductive age and from 2 to

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5 per cent in postmenopausal women[2-5]. The majority of patients with endometriosis are asymptomatic, and only 6-10 per cent of them suffer from pelvic pain[6]. This chronic gynaecological disease is accompanied with different symptoms such as chronic pelvic pain, dyschezia, lower back pain, dyspareunia, infertility and dysmenorrhoea[7]. Epidemiological indicators such as prevalence can be useful for healthcare managers and policymakers. Thus, a systematic review and meta-analysis was undertaken to provide an estimation of the prevalence of endometriosis in women.

Material & Methods

Search strategy: All international databases including MEDLINE, Web of Science, Google scholar, Scopus and Cumulative Index to Nursing and Allied Health Literature were searched for the original articles without language and time limitation, written from January 1990 to December 2018. Keywords were searched electronically by two independent Boolean operators using a specified search strategy. The protocol of this study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42017075275)[8].

Inclusion/exclusion criteria: Two reviewers independently carried out the literature search and evaluation of the searched articles based on the inclusion and exclusion criteria. The structures of the searched articles were appraised by the reconstructed PRISMA checklist[9]. All the articles with full text in English conducted as a cross-sectional design reporting the prevalence of endometriosis in any stage of the disease in women aged 15-60 yr old, were include.

Data extraction: Using a uniform excel sheet, two reviewers independently extracted the required data from the data contained in the identified articles. Discrepancies in the extracted data were resolved through consensus, and if agreement could not be reached, they resolved it by referral to a third investigator. The STROBE checklist[10] was used as a standard checklist for reporting the results of the included studies.

Quality assessment and risk of bias: The quality of each study was assessed according to the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[11] which included the quality of research question, study population, sampling strategy, groups recruited from the same population and uniform eligibility criteria, sample size justification, exposure assessed before outcome measurement, sufficient timeframe to observe an effect, different levels of the exposure of interest, exposure measurement and assessment, repeated exposure assessment, outcome measurement, blinding of outcome assessors, follow up rate and statistical analyses. This tool measures 14 different criteria which are used to give each study an overall quality rating of good, fair or poor.

Statistical analysis: Random effects models were used based on the presence of heterogeneity. Heterogeneity was assessed using Q Cochran's test and I^2 index[12]. The forest plot was implemented for showing the results of the individual and pooled effects of all the studies. The Egger's test was also used to evaluate the presence of publication bias[12]. In addition, a subgroup analysis was done (by sample size, stages of endometriosis, diagnostic method, continent and clinical symptoms) to identify different sources of heterogeneity. A $P<0.05$ was considered significant for all statistical tests, except for Q Cochran's, meta-regression and Egger's test (<0.1). All statistical analyses were performed through STATA version 12.0 (STATA Corp., College Station, TX, USA).

Results

A total of 2433 articles were extracted for this study. Finally, 17 studies[13-29] with 127,476 women suffering from endometriosis were included for estimating the prevalence of endometriosis (Fig. 1). The characteristics of the included studies are described in Table I. The quality assessment details for the included studies are shown in Table II.

A meta-analysis was conducted regarding the stage of the disease, diagnostic method, continent and clinical symptoms to estimate the prevalence of endometriosis. The pooled prevalence estimate of endometriosis regardless of the stage of disease, diagnostic method, continent and clinical symptoms was 18 per cent [95% confidence interval (CI): 16-20; Fig. 2]. The prevalence of endometriosis based on the stage of the disease ranged from two per cent (95% CI: 1-4) for stage 4 to 20 per cent (95% CI: 11-28) for stage 1 (Table III).

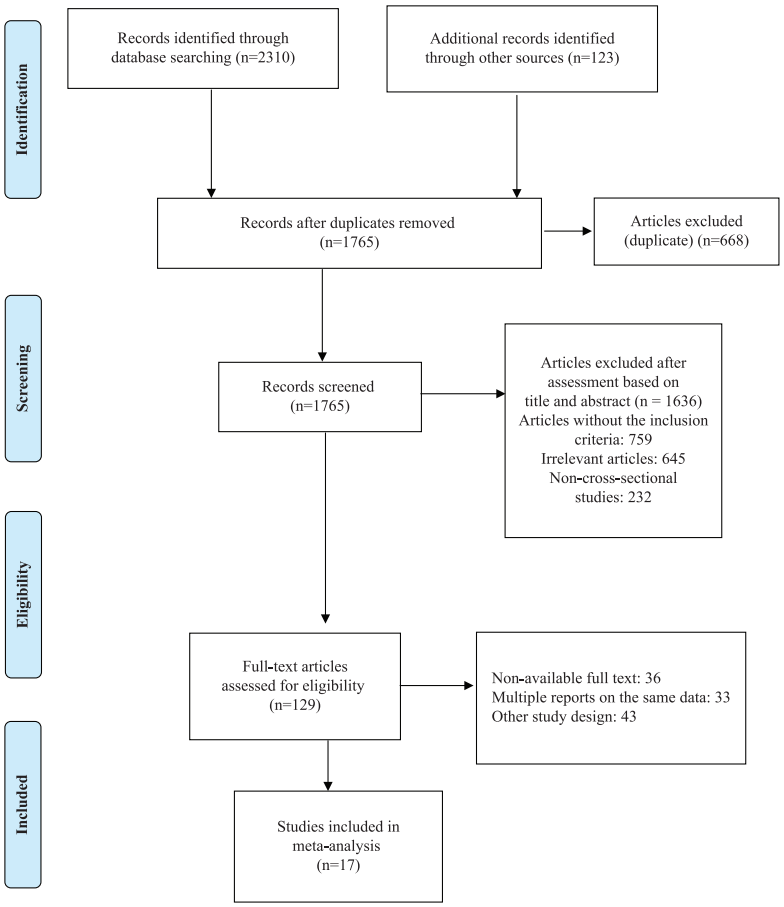

Fig. 1. Flow diagram showing literature search and study selection.

The prevalence of endometriosis by the diagnostic method ranged from 12 per cent (95% CI: 3-21) for endometriosis diagnosed with other diagnostic methods to 20 per cent (95% CI: 17-22) for endometriosis diagnosed with laparoscopic method (Table III). The CI of Egger's test did not include zero, showing significant publication bias (Fig. 3). Furthermore, high statistical heterogeneity (I^2>99%, P<0.001) was identified in total analyses (Table III).

The prevalence of endometriosis by the continent ranged from 17 per cent (95% CI: 12-21) for Europe to 36 per cent (95% CI: 5-69) for Asia, and by the sample size ranged from 28 per cent (95% CI: 19-37) for studies with less than of 1000 individuals to seven per cent (95% CI: 3-11) for studies with more than of 1000 individuals (Table III). The results of subgroup analysis indicated that the prevalence rates of endometriosis in women with infertility, chronic pelvic pain and asymptomatic women were 31 (95% CI: 15-48), 42 (95% CI: 25-58) and 23 per cent (95% CI: 19-26), respectively (Table III).

Meta-regression was used to explore the sources of between-study heterogeneity including age and diagnostic method. According to the results, the prevalence of endometriosis did not show a relationship with age (P>0.10) and diagnostic method (P>0.10).

Discussion

Regarding the stage of endometriosis, the results of this study showed that the prevalence of minimal endometriosis (stage 1) was higher than other stages of endometriosis. Considering the diagnostic method, the prevalence of endometriosis diagnosed with laparoscopy, ultrasound and magnetic resonance imaging (MRI) methods was higher than endometriosis diagnosed with other diagnostic methods in the world. Another study showed the same results[30].

The precise prevalence of endometriosis in female adult population is not known. The prevalence in fertile women undergoing sterilization is four per cent (1.5-

Table I. Characteristics of the included studies

Authors	Publication year	Data collection year	Country	Age (yr)	Sample size	Study population	Diagnostic method	Prevalence (%)				
								All stages	Stage 1	Stage 2	Stage 3	Stage 4
Moen and Muus[12]	1991	1986-1989	Norway	20-50	208	Asymptomatic women	Laparoscopic	19.23	19.23	0.93	-	0.93
Waller *et al*[13]	1993	1990-1992	United Kingdom	21-45	174	Asymptomatic women	Laparoscopic	32.2	22.98	7.47	1.72	-
Melis *et al*[14]	1994	1991-1993	Italy	15-57	305	Asymptomatic women	Laparoscopic	24.9	9.15	26.2	7.86	5.24
Chu *et al*[15]	1995	1993	Taiwan	-	752	Asymptomatic women	Laparoscopic	32.5	-	-	-	-
Laufer *et al*[16]	1997	1990-1994	USA	13-21	46	Women with chronic pelvic pain	Laparoscopic	69.6	77.4	22.6	-	-
Oral *et al*[17]	2003	1995-2001	Turkey	26-70	183	Malignant epithelial ovarian tumours	Histopathological criteria	7.65	4.37	4.37	3.27	-
Darwish *et al*[18]	2006	1998-2005	Egypt	-	2493	Women with chronic pelvic pain	Laparoscopic	18.8	34.9	39.6	10.3	15.2
Zacharia and O'Neill[19]	2006	2000-2003	USA	32-54	59	Asymptomatic women	MRI	34	-	-	-	-
Ferrero *et al*[20]	2010	2007-2009	Italy	<50	1291	Infertile women	Ultrasound	3.6	-	-	-	-
Camilleri *et al*[21]	2011	2003-2008	Malta	-	437	Infertile women	Laparoscopic	16.9	8.69	-	1.37	0.91
Abbas *et al*[22]	2012	2007	Germany	15-54	62323	Infertile women	Laparoscopic	0.81	-	-	-	-
Fawole *et al*[23]	2015	2008-1010	Nigeria	18-45	245	Asymptomatic women (in women with chronic pelvic pain=55.8%)	Laparoscopic	48.1	-	-	-	-
Ragab *et al*[24]	2015	2012-2014	Egypt	-	654	Girls with severe dysmenorrhoea	Ultrasonography/ laparoscopy/MRI	12.3	5.45	3.18	3.63	-
Umelo and Manchanda[25]	2015	2012-2014	Indian	15-49	440	Asymptomatic women (infertile women=87.3% and in women with chronic pelvic pain=56.4%)	Laparoscopic	25	7.3	35.5	31.8	25.1
Fuldeore and Soliman[26]	2016	2012	USA	18-49	48020	Asymptomatic women	Laparoscopic	6.1	-	-	-	-
Boujenah *et al*[27]	2017	2007-2015	France	-	52	Infertile women	Ultrasonography/ laparoscopy/MRI	50	-	-	-	-
Eisenberg *et al*[28]	2017	1998-2015	Israel	15-55	6146	Asymptomatic women	Laparoscopic	1.1	-	-	-	-

MRI, magnetic resonance imaging

Table II. Quality assessment of included articles based on Quality Assesment Tool for observational cohort & cross-sectional studies[11].

Authors	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Quality rating	STROBE score
Moen and Muus[12]	Yes	Yes	Yes	NR	NR	NR	Yes	NA	Yes	No	Yes	No	No	No	Fair	16
Waller *et al*[13]	Yes	Yes	NR	Yes	No	No	NA	NA	Yes	No	Yes	NR	NR	NA	Fair	18
Melis *et al*[14]	Yes	Yes	Yes	NR	NA	NR	NR	NR	NA	NR	NA	NR	NR	NR	Poor	4
Chu *et al*[15]	Yes	Yes	Yes	Yes	NR	NA	NR	NR	NR	NA	Yes	NR	NR	NR	Fair	13
Laufer *et al*[16]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	NR	NR	Good	20
Oral *et al*[17]	Yes	Yes	Yes	Yes	NA	NR	NR	NA	NR	NR	Yes	NA	NR	NR	Fair	2
Darwish *et al*[18]	Yes	Yes	Yes	NR	NR	No	NR	NR	No	No	Yes	NR	NR	No	Poor	17
Zacharia and O'Neill[19]	Yes	No	NR	Yes	NR	NA	NA	NA	NA	NA	Yes	NR	NR	No	Poor	22
Ferrero *et al*[20]	Yes	Yes	Yes	Yes	NR	NR	NR	NR	NR	NR	Yes	NR	NR	NR	Fair	22
Camilleri *et al*[21]	Yes	Yes	NA	NR	No	NA	NR	NA	NA	NR	No	NA	NA	NA	Poor	12
Abbas *et al*[22]	Yes	Yes	Yes	Yes	NA	NR	NR	NR	NR	NA	Yes	NA	NA	NA	Fair	21
Fawole *et al*[23]	Yes	Yes	NR	Yes	No	NR	NR	NR	NR	NR	Yes	NA	NA	NA	Poor	20
Ragab *et al*[24]	Yes	Yes	NA	NR	NA	NA	NR	NA	NA	NA	Yes	NA	NR	NA	Poor	18
Umelo and Manchanda[25]	Yes	Yes	Yes	NR	NR	NR	NA	NR	NR	NA	Yes	NR	NR	NR	Poor	16
Fuldeore and Soliman[26]	Yes	Yes	No	Yes	No	NR	NA	NR	NR	NA	No	NA	NA	NA	Poor	25
Boujenah *et al*[27]	Yes	Yes	NA	Yes	No	No	NA	NA	Yes	No	Yes	NA	NA	NA	Fair	18
Eisenberg *et al*[28]	Yes	Yes	No	NR	NA	NA	NA	NR	NR	NR	Yes	NA	NA	NR	Poor	21

CD, cannot determine; NA, not applicable; NR, not reported

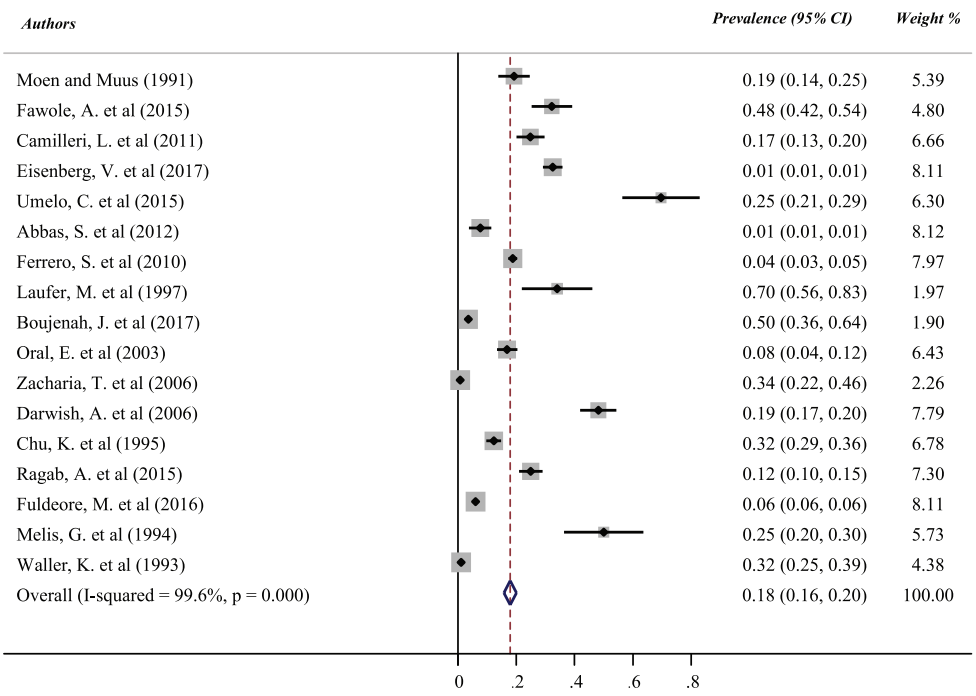

Fig. 2. Pooled prevalence estimate of endometriosis.

Table III. Pooled prevalence estimates along with 95% confidence intervals of endometriosis by stage of disease, diagnostic method and continent

Subgroups	Number of studies	Prevalence estimate (%) (95% CI)	Between subgroups		Between groups	
			I^2 (%)	$P_{heterogeneity}$	Q	$P_{heterogeneity}$
Stages						
1	9	20 (11-28)	99.10	0.001	16.44	0.001
2	8	13 (7-18)	99.60	0.001		
3	7	5 (2-8)	97.00	0.001		
4	5	2 (1-4)	84.30	0.001		
Clinical symptoms						
Infertility	5	31 (15-48)	99.10	0.001	20.21	0.001
Chronic pelvic pain	4	42 (25-58)	99.20	0.001		
Asymptomatic women	9	23 (19-26)	99.00	0.001		
Ovarian malignancy	1	-	-	-		
Diagnostic method						
Laparoscopy	12	20 (17-22)	99.70	0.001	13.23	0.001
Other (ultrasound or MRI or histopathology)	3	12 (3-21)	92.80	0.001		
Laparoscopy, ultrasound and MRI	2	31 (25-37)	96.50	0.001		
Total	17	18 (16-20)	99.60	0.001		
Continent						
Europe	8	17 (12-21)	98.20	0.001	17.98	0.001
Americas	3	19 (3-36)	99.60	0.001		
Asia	3	36 (5-69)	96.10	0.001		
Africa	3	26 (14-38)	98.20	0.001		
Total	17	18 (16-20)	99.60	0.001		
Sample size						
<1000	13	28 (19-37)	99.00	0.001	19.09	0.001
>1000	4	7 (3-11)	99.90	0.001		
Total	17	18 (16-20)	99.60	0.001		

*P<0.05. MRI, magnetic resonance imaging; CI, confidence interval

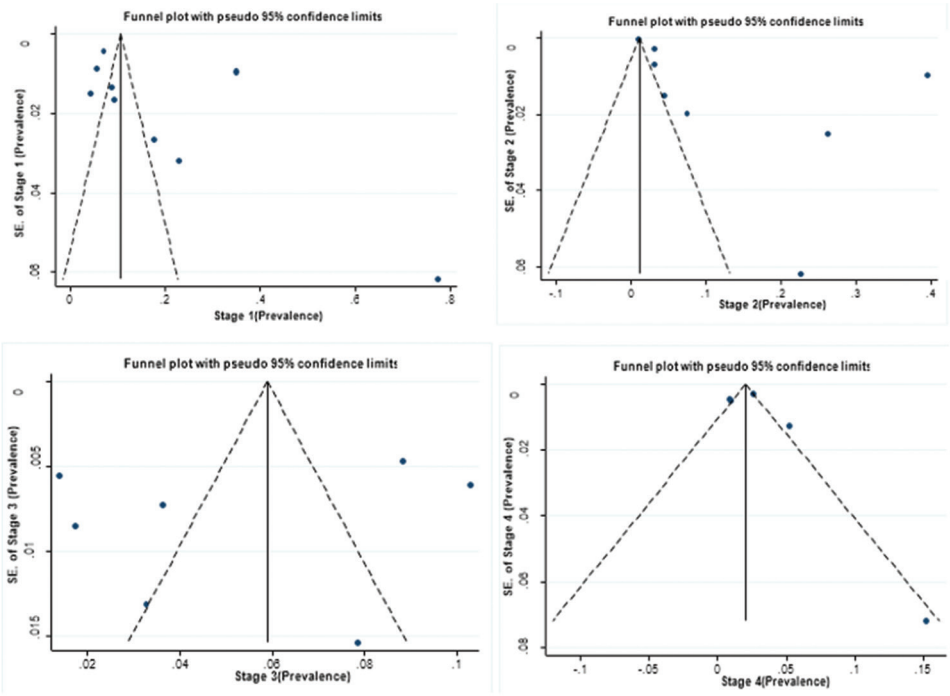

Fig. 3. Funnel plot for pooled prevalence estimate by different stages of endometriosis.

5%), whereas it is 13.5 per cent (2-68%) in infertile women[5]. The reported prevalence of this disease in women undergoing laparoscopy for chronic pelvic pain ranged from 15 to 75 per cent[6]. A study conducted in north India in 2015 showed that the precise prevalence of endometriosis was not known; however, it was estimated to be 2-10 per cent in the general population, but up to 50 per cent in infertile women[31].

Endometriosis affects approximately 70 per cent of women with dysmenorrhoea and dyspareunia[32]. Adolescents may have more severe symptoms. Reports from Germany showed that 0.05, 1.93 and 6.1 per cent of the patients were in the age groups of 10-14, 15-19 and 20-24 yr, respectively[33-35]. A review of previous studies indicated that global estimates varied significantly and ranged from approximately 2-45 per cent based on the diagnostic criteria and the study population[35]. The world statistics suggest that 10-15 per cent of women in the world are affected by endometriosis, which is consistent with the results of our study, as the overall prevalence was estimated to be 18 per cent[35]. According to our analysis, the prevalence of endometriosis in developing countries was higher than in developed countries as also shown by another study[36].

The present study had several limitations. First, the number of studies in some subgroups was small and did not provide sufficient statistical power to assess the source of heterogeneity. Second, there were some other factors (such as diagnostic accuracy, quality of detective equipment and physicians' skills in detecting endometriosis) that might be important sources of heterogeneity, but we could not evaluate their role in heterogeneity due to the lack of information. Third, some of the included studies did not measure the variables such as age or prevalence of endometriosis by the stage of the disease.

Despite the high heterogeneity of the studies, this systematic review and meta-analysis showed a high prevalence of endometriosis in developing countries. The prevalence of endometriosis in women with chronic pelvic pain was higher than those with infertility. Future studies are needed to explore factors affecting endometriosis prevalence worldwide, which may help develop future prevention programmes.

***Financial support & sponsorship*:** None.

***Conflicts of Interest*:** None.

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