QUALITY OF LIFE IN WOMEN WITH ENDOMETRIOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract - Endometriosis is a common gynecological disease which affects different aspects of women's life in reproductive ages. The objective of this meta-analysis was to investigate the effect of endometriosis on the affected patients' quality of life (QoL). PubMed, Medline, Embase, Science direct, CINAHL, Cochrane Clinical Trials, Magiran and SID were searched up to November, 19, 2016. The studies using Endometriosis Health Profile-30 (EHP-30) to evaluate QoL in women with endometriosis were selected. A total of 7 studies (1619 cases) which satisfied the inclusion criteria were included in the meta-analysis. The QoL scores in the 5 dimensions of core questionnaire were ranged from 43.70 to 56.14 and in 6 dimensions of the optional modular questionnaire from 30.27 to 59.26. These results confirmed that the endometriosis imposes a considerable burden of QoL on the affected women.

KEYWORDS: Endometriosis, Quality of life, Pelvic pain, Endometriosis health profile.

INTRODUCTION

Endometriosis is a common chronic inflammatory estrogen-related disease which affects women in reproductive ages¹⁻⁴. This condition is characterized by abnormal positioning of endometrial glands and stroma outside the uterine². Endometriosis has a multifactorial etiology including genetic predisposition and immune system abnormalities as same as anatomical and environmental factors⁵.

The prevalence rate of endometriosis in general population is unknown because the definitive diagnosis of the condition is possible by laparoscopic surgery, therefore many cases are not recognized. However, various studies have reported 2-15% prevalence of endometriosis among the reproductive ages women^{2,3,6-12}. Also, studies have shown that 30-45% of women with infertility or pain are suffering from endometriosis¹². Endometriosis can be staged I-IV by the classification of the American Society of Reproductive Medicine (ASRM) based

on the location, extent, and depth of endometrial implants, presence and severity of adhesions and ovarian endometriomas size which called minimal, mild, moderate, and severe endometriosis^{2,5}.

Endometriosis has a variety of symptoms including chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, lower abdominal pain, infertility and others such as diarrhea or constipation, chronic fatigue, nausea and vomiting, headaches, heavy and/or irregular periods and hypoglycemia-menstrual pain^{2,7,13}. About two-third of women with endometriosis are suffering from chronic pelvic pain, and 30-40% of them are experiencing infertility. It is said that the prevalence of infertility in women affected by endometriosis is 20 times more than those without this condition. Despite recent improvements in the treatment of gynecological diseases, so far no treatment has been found for endometriosis².

The chronic painful symptoms of endometriosis and its negative consequences can also severely re-

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duce the affected women's quality of life. Qualitative studies have documented the negative impacts of this disease on daily life; physical, mental and social well-being; general health; interpersonal interactions; productivity and self-esteem^{2,4,6,7,12,14-17}. So, endometriosis symptoms are among the main causes of morbidity and psychosocial problems of women of reproductive ages. Chronic pain may lead to a feeling of frustration, social dysfunction, and difficulties in work. Infertility caused by endometriosis, as well as a delay in diagnosis, can also lead to frustration and isolation¹⁸. The negative effects of endometriosis on the sexual relationship could disrupt the familial relations. Therefore, endometriosis has severe psychological burden. Some studies^{2,4,8,15,19} have shown that endometriosis is threatening mental health in a way that psychological interventions could be suggested for patients^{6,7,10}. So, in recent years, some studies have investigated the effects of endometriosis on the quality of life (QoL) or health-related quality of life (HRQoL). The quality of life is a multidimensional and dynamic concept that includes physical, social and mental aspects of health which is associated with a particular disease or its treatment^{2,7,19}. In this regards, various instruments have been designed in order to assess the impact of endometriosis on quality of life and health-related quality of life including Endometriosis Health Profile-30 (EHP-30) and its short form EHP-5, SF-36, SF-12, EQ -5D, Duke health profile, EuroQoL WQ-5D, Nottingham health profile and HRQoL instrument for Symptomatic patients with endometriosis^{4,14,15,19}, but in recent years EHP-30 was the most widely used instrument in the studies.

This questionnaire was developed in the UK in 2001 by Jones et al. through exploratory interviews with women who had surgically confirmed endometriosis. The questionnaire is a self-reported instrument which contains a core questionnaire with 30 items in 5 dimensions (pain, control and powerlessness, emotional well-being, social support and self-image) and an optional modular questionnaire with 23 items in 6 dimensions (work, relationship with child/children, sexual relationship, feelings about medical profession, feelings about treatment and feelings about infertility) that may not apply to every woman.

Each scale is scored on a scoring system ranging from 0-100 in which the lower the score the better the patient's QoL^{6,7,14,18}. Jones et al²⁰ and Jones et al⁹, investigated again in the UK the responsiveness and data quality, scale reliability, response rates and scaling assumptions of EHP-30. To date, different versions of EHP-30 as the Iranian, Dutch, Portuguese, Portuguese-Brazilian, American, Chinese, Italian and Australian have been also validated^{6,21-24}. ASRM and European society of human reproductive

and embryology also have recommended this questionnaire to measure the quality of life in women with endometriosis. Therefore, EHP-30 has widely used for the measurement of QoL and HRQoL in women with endometriosis. Although some authors have conducted reviews on these studies²⁵⁻²⁹, rare meta-analysis have been published.

Therefore, in this study, we tried to conduct a meta-analysis of published studies on the effects of endometriosis on QoL using EHP-30.

PATIENTS AND METHODS

Data sources and search strategy

A comprehensive literature search was performed in Medline/ PubMed, Embase, Science direct, CINAHL, Cochrane Clinical Trials, Magiran and SID up to November, 19, 2016 using the text search terms "quality of life", "health-related quality of life", "pelvic pain", "endometriosis health profile", "quality of life measurement" in combination with "endometriosis" and their Persian equivalents. Additional articles were identified by manually searching of the references of retrieved eligible articles. No restrictions of language, date or geographical location were placed.

Inclusion criteria

Peer reviewed journal articles that examined the effect of surgically and/or histologically diagnosed endometriosis on the QoL using EHP-30 were included in this meta-analysis.

Exclusion criteria

Studies that have reported the prevalence or clinical features of endometriosis or the effectiveness of endometriosis treatments were excluded. Reviews, opinion pieces, commentaries and case studies were excluded. Studies which used other instruments for measuring the quality of life were also excluded.

Screening

Studies identified through databases searching were screened for eligibility. First, duplicates were removed. Following this, titles and, if needed, abstracts and full texts were screened by 3 authors independently (K.Ch-A, E.B, M.A.B) based on defined inclusion and exclusion criteria and ineligible ones were removed.

Methodological quality assessment

All studies meeting the selection criteria were assessed for their methodological quality using a quality assessment checklist (Moosazadeh et al)³⁰, which has been designed based on the STROBE checklist (Von Elm et al)³¹. This checklist includes questions related to different aspects of a study including the study design, type of study, sample size, objectives, study population, inclusion and exclusion criteria, samples matching method, analyzing method and appropriate reporting of results based on the objectives in which for each question a score has been considered and any study that obtains at least 8 scores is selected for including in meta-analysis.

Data Extraction

Studies which met the inclusion criteria and passed the methodological quality assessment were examined comprehensively and needed data was collected in an Excel data spreadsheet recording: first author, publication date, research coun-

try, study design, sample size, participants mean age and key findings of EHP-30 core questionnaire and optional modular questionnaire. The data spreadsheet was completed by one author (M.A.B), and all other authors verified the data extraction.

ANALYSIS

Gathered Data was analyzed by using STATA ver.11 software. The heterogeneity index between studies was investigated trough Cochran (Q) and I-squared tests. The Egger test was used for the investigation of the publication bias of results.

RESULTS

Our research retrieved a total number of 27658 studies from which 7 studies met the eligibility and inclusion criteria to be included in the meta-analysis. Figure 1 shows the selection process of these studies. Figure 2 to Figure 11 present the mean

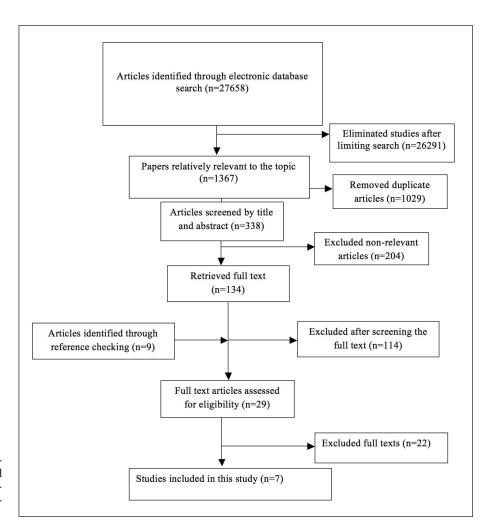


Fig. 1. Flow diagram showing the literature review and selection process of the studies included in the metanalysis.

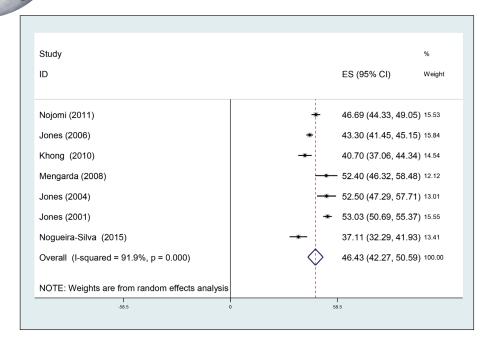


Fig. 2. Mean scores and the overall estimation of pain dimension of EHP-30 core questionnaire.

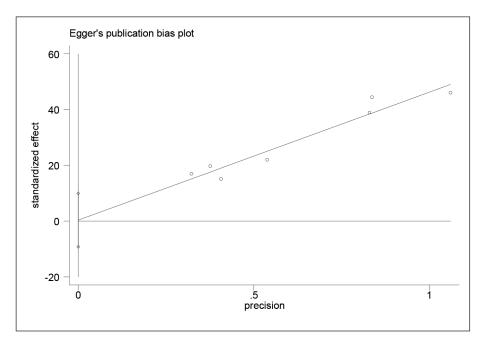


Fig. 3. The egger test results for the investigation of publication bias of pain.

scores of 5 core dimensions of EHP-30 in the primary studies, the total estimation and the egger test for investigating the publication bias of results.

As shown in the above figure the estimated score of pain for the endometriosis patients is 46.43, which shows the high burden of this dimension for the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 74.44 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 91.9%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age)

showed that this variable has not effect on the heterogeneity (B=-0.8, p=0.470). Also, the Egger test showed that the publication bias is not statistically significant for pain (B=0.3, p=0.933) (Figure 3).

As shown in the above figure the estimated score of control and powerlessness for the endometriosis patients is 56.14, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 353.89 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 98.3%

Fig. 4. Mean scores and the overall estimation of control and powerlessness dimension of EHP-30 core questionnaire.

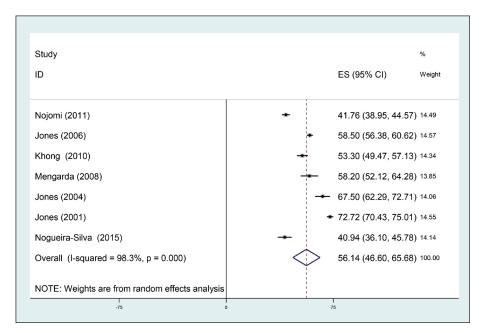
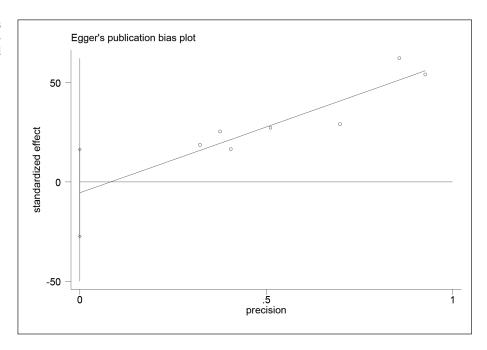


Fig. 5. The egger test results for the investigation of publication bias of control and powerl



The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-3.2, p =0.105). Also, the Egger test showed that the publication bias is not statistically significant for control and powerlessness (B=-5.5, p =0.549) (Figure 5).

As shown in the above figure the estimated score of emotional well-being for the endometriosis patients is 48.31, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 66.87 (d.f. = 6) *p* = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 91.0%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-1.003, p =0.292). Also, the Egger test showed that the publication bias is not statistically significant for emotional well-being (B=-1.6, p =0.654) (Figure 7).

As shown in the above figure the estimated score of social support for the endometriosis pa-

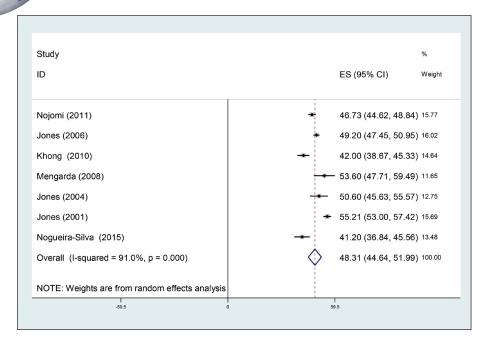


Fig. 6. Mean scores and the overall estimation of emotional well-being dimension of EHP-30 core questionnaire.

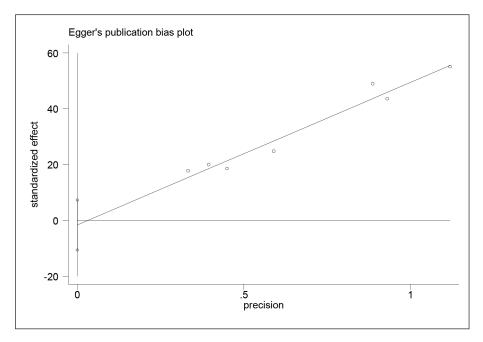


Fig. 7. The egger test results for the investigation of publication bias of emotional wellbeing.

tients is 49.52, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 158.53 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 96.2%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-2.3, p =0.134). Also, the Egger test showed that the publication bias is not statistically significant for social support (B=-3.8, p =0.562) (Figure 9).

Fig. 8. Mean scores and the overall estimation of social support dimension of EHP-30 core questionnaire.

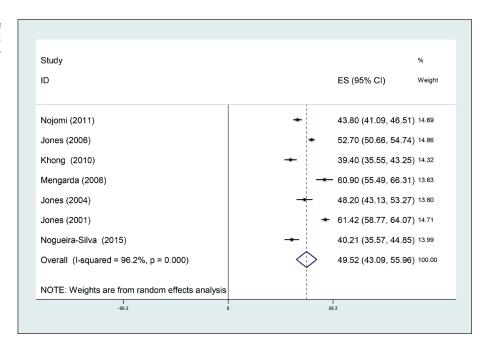
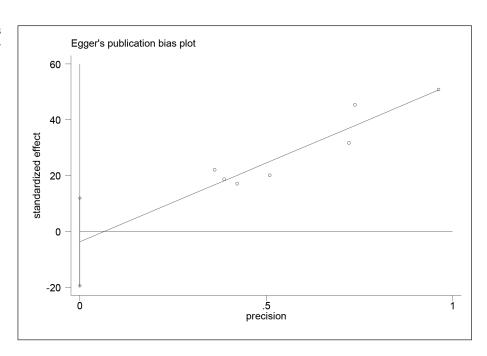


Fig. 9. The egger test results for the investigation of publication bias of social support.



As shown in the above figure the estimated score of self-image for the endometriosis patients is 43.70, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 162.89 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 96.3%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-2.1, p =0.142). Also, the Egger test showed that the publication bias is not statistically significant for self-image (B=1.9, p =0.737) (Figure 11).

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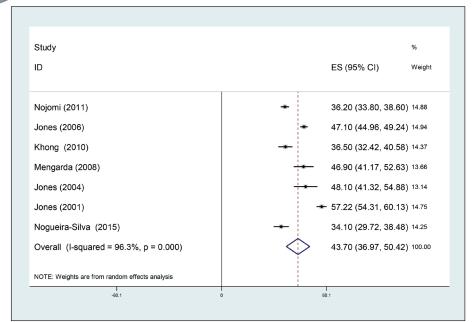


Fig. 10. Mean scores and the overall estimation of self-image dimension of EHP-30 core questionnaire.

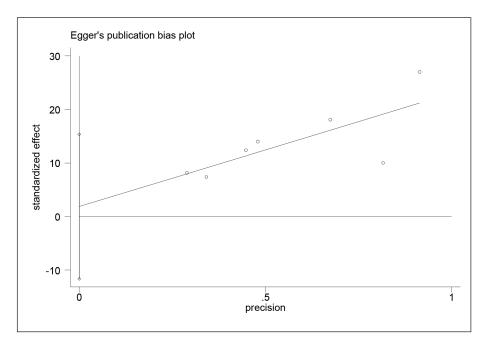


Fig. 11. The egger test results for the investigation of publication bias of social support.

Fig. 12. Mean scores and the overall estimation of work dimension of EHP-30 modular questionnaire.

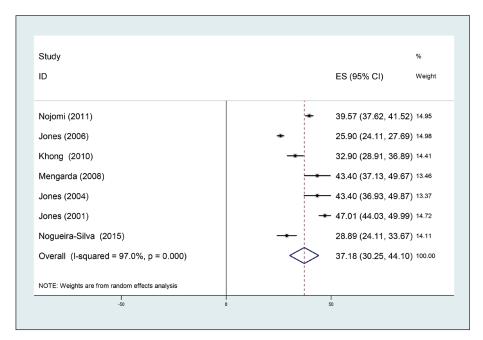
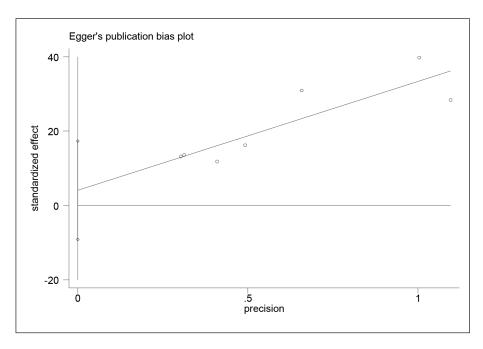


Fig. 13. The egger test results for the investigation of publication bias of work.



Also, Figure 12 to Figure 23 present the mean scores of 6 optional modular dimensions of EHP-30 in the primary studies, the total estimation and the egger test for investigating the publication bias of results.

As shown in the above figure the estimated score of work for the endometriosis patients is 37.18, which shows the moderate burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 203.29 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 97.0%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-0.8, p =0.611). Also, the Egger test showed that the publication bias is not statistically significant for self-image (B=4.1, p =0.464) (Figure 13).

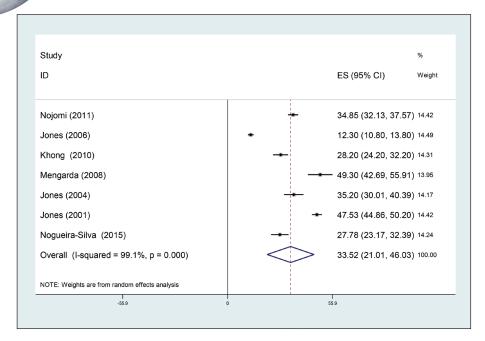


Fig. 14. Mean scores and the overall estimation of relationship with children dimension of EHP-30 modular questionnaire.

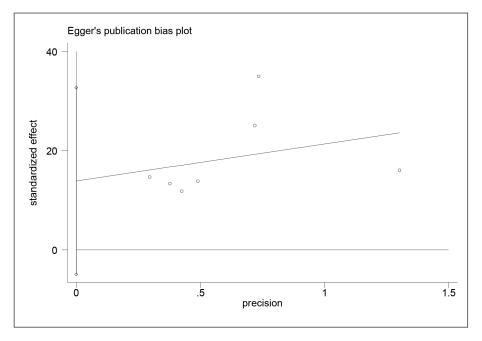


Fig. 15. The egger test results for the investigation of publication bias of relationship with children.

As shown in the above figure the estimated score of relationship with children for the endometriosis patients is 33.52, which shows the moderate burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 668.27 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 99.1%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-1.9, p =0.420). Also, the Egger test showed that the publication bias is not statistically significant for relationship with children (B=13.8, p =0.116) (Figure 15).

As shown in the above figure the estimated score of sexual intercourse for the endometriosis patients is 51.75, which shows the high burden of this dimen-

Fig. 16. Mean scores and the overall estimation of sexual intercourse of EHP-30 modular questionnaire.

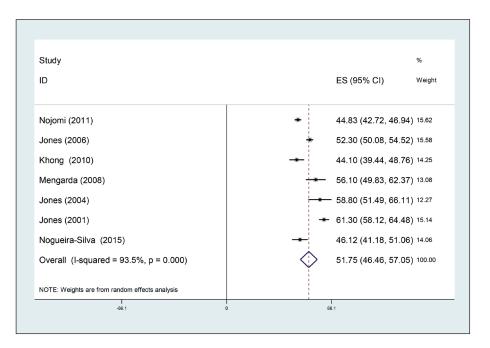
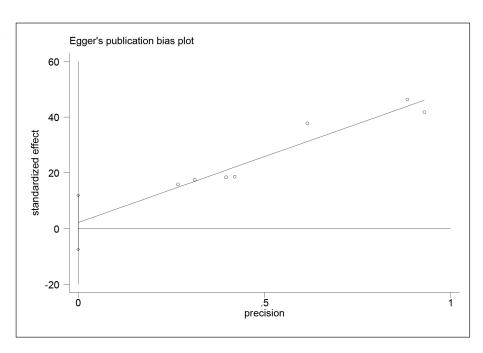


Fig. 17. The egger test results for the investigation of publication bias of sexual intercourse.



sion on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 92.77 (d.f. = 6) *p* = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 93.5%

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-1.9, p = 0.094). Also, the Egger test showed that the publication bias is not statis-

tically significant for sexual intercourse (B=2.2, *p* =0.591) (Figure 17).

As shown in the above figure the estimated score of medical profession for the endometriosis patients is 30.27, which shows the moderate burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 199.71 (d.f. = 6) *p* = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 97.0%

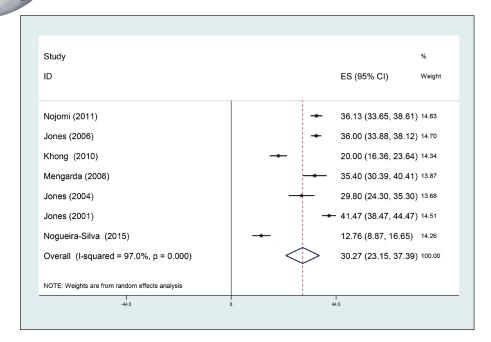


Fig. 18. Mean scores and the overall estimation of medical profession of EHP-30 modular questionnaire.

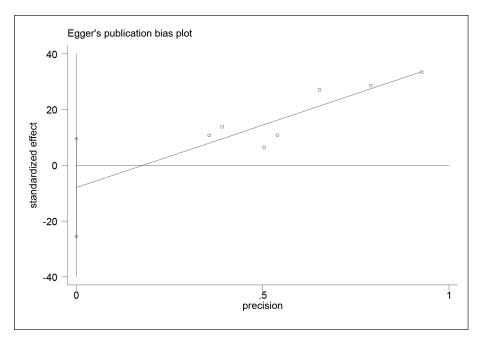


Fig. 19. The egger test results for the investigation of publication bias of medical profession.

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-0.3, p =0.893). Also, the Egger test showed that the publication bias is not statistically significant for medical profession (B=-8.03, p=0.293) (Figure 19).

As shown in the above figure the estimated score of treatment for the endometriosis patients

is 47.58, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 219.29 (d.f. = 6) p = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 97.3%

Fig. 20. Mean scores and the overall estimation of treatment of EHP-30 modular questionnaire.

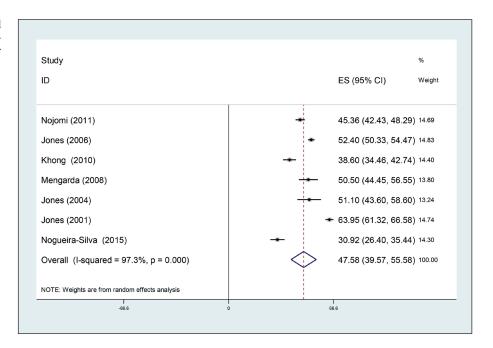
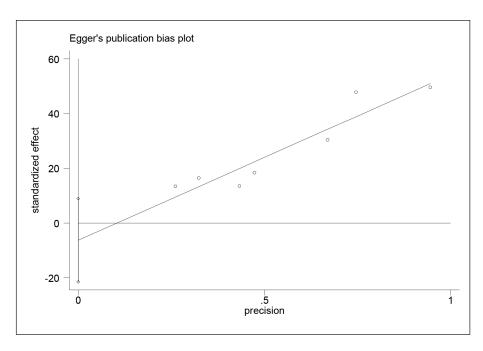


Fig. 21. The egger test results for the investigation of publication bias of treatment.



The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-1.5, p =0.436). Also, the Egger test showed that the publication bias is not statistically significant for treatment (B=-6.3, p=0.334) (Figure 21).

As shown in the above figure the estimated score of infertility for the endometriosis patients

is 56.26, which shows the high burden of this dimension on the patients' QoL. The results of heterogeneity test for this dimension are as following:

- Heterogeneity chi-squared = 83.73 (d.f. = 6) *p* = 0.000
- I-squared (variation in ES attributable to heterogeneity) = 92.8%

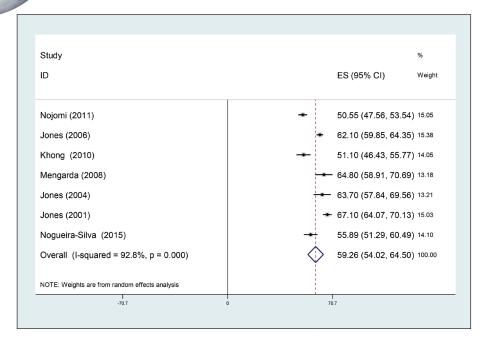


Fig. 22. Mean scores and the overall estimation of infertility of EHP-30 modular questionnaire.

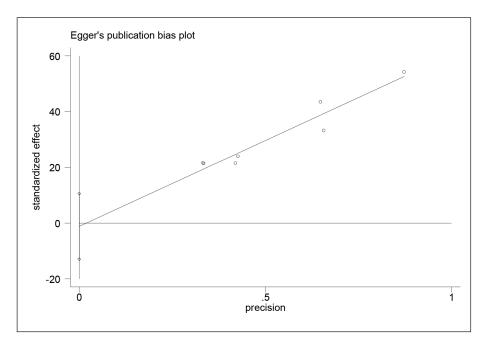


Fig. 23. The egger test results for the investigation of publication bias of infertility.

The meta-regression results for the investigation of the probable source of heterogeneity (mean age) showed that this variable has not effect on the heterogeneity (B=-2.1, p=0.041). Also, the Egger test showed that the publication bias is not statistically significant for infertility (B=-1.2, p=0.799) (Figure 23).

DISCUSSION

This study was aimed to analysis the results of primary studies on the effect of endometriosis on patients' QoL. For this purpose, 7 primary studies were included in the meta-analysis. Only studies which used the EHP-30 for measuring QoL were analyzed. Mean scores of 5 core dimensions of EHP-30 included studies and the overall estimations are followings:

- Pain: Mean pain scores are ranging from 37.11 to 53.03 in the primary studies. Overall estimation of this dimension is as 46.43.
- Control and powerlessness: Mean scores of control and powerlessness are ranging from 40.94 to 72.72 in the primary studies. Overall estimation of this dimension is as 56.14.

TABLE 1. Main characteristics of primary studies and mean scores of core questionnaire dimensions.

Author/s	Publication date	Country	Sample size	Mean age of participants	Pain	Control and power-lessness	Emotional well-being	Social support	Self-image
Nojomi et al ⁸	2011	Iran	100	39.5±7.54	46.69±12.04	41.76±14.33	46.73±10.75	43.8±13.85	36.2±12.25
Jones et al ⁹	2006	UK	727	34.7±8.15	43.3 ± 25.4	58.5 ± 29.1	49.2 ± 24.1	52.7±28	47.1±29.5
Khong et al ¹⁵	2010	Australia	195	34.6±7.6	40.7±25.9	53.3±27.3	42±23.7	39.4±27.4	36.5 ± 29.1
Mengarda et al ²¹	2008	Brazil	54	31.8 ± 4.9	52.4 ± 22.8	58.2 ± 22.8	53.6 ± 22.1	60.9 ± 20.3	46.9 ± 21.5
Jones et al ²⁰	2004	UK	99	34.3±6	52.5 ± 21.6	67.5 ± 21.6	50.6 ± 20.6	48.2±21	48.1 ± 28.1
Jones et al ¹⁸	2001	UK	325	32.5±7.2	53.03 ± 21.51	72.72 ± 21.04	55.21 ± 20.33	61.42 ± 24.42	57.22 ± 26.74
Nogueira-Silva et al ⁷	2015	Portugal	152	34.7±6.1	37.11 ± 30.32	40.94 ± 30.43	41.2±27.43	40.21 ± 29.17	34.1±27.57

- Emotional well-being: Mean scores of emotional well-being are ranging from 41.2 to 55.21. Overall estimation of this dimension is as 48.31
- Social support: Mean social support scores are ranging from 39.4 to 61.42 in the primary studies. Overall estimation of this dimension is as 49.52
- Self-image: Mean scores of self-image are ranging from 34.1 to 57.22 in the primary studies. Overall estimation of this dimension is as 43.70^{7-9,15,18,20,21}.

These mean scores of all primary studies and the overall estimation of the meta-analysis show that endometriosis has a moderate to high negative effect on the QoL in all core dimensions of EHP-30.

Also, from 7 included studies, control and powerlessness in 4 studies, emotional well-being in 2 studies and social support in one study have the highest mean score and show the most negative effect on the QoL. In the overall estimation of meta-analysis, also, control and powerlessness were founded as the most negatively affected aspect of QoL from endometriosis. In return, self-image in 5 studies and pain in 2 studies have the lowest mean scores and show the least negative effect on the QoL^{7-9,15,18,20,21}. In the overall estimation of meta-analysis, also, self-image was found as the least negatively affected aspect of QoL due to the endometriosis.

Our other findings indicate that the mean scores of 6 optional modular dimensions of EHP-30 and their overall estimations are as followings:

- Work: Mean work scores are ranging from 25.9 to 47.1 in the primary studies. Overall estimation of this dimension is as 37.18.
- Relationship with children: Mean scores of relationship with children are ranging from 12.3 to 49.3 in the primary studies. Overall estimation of this dimension is as 33.52.
- Sexual intercourse: Mean scores of sexual intercourse are ranging from 44.1 to 61.3 in the primary studies. Overall estimation of this dimension is as 51.75.
- Medical profession: Mean scores of the medical profession are ranging from 12.76 to 41.47 in the primary studies. Overall estimation of this dimension is as 30.27.
- Treatment: Mean scores of treatment are ranging from 30.92 to 63.95 in the primary studies. Overall estimation of this dimension is as 47.58.
- Infertility: Mean scores of infertility are ranging from 50.55 to 67.1 in the primary studies. Overall estimation of this dimension is as 59.26^{7-9,15,18,20,21}.



TABLE 2. Mean scores of optional modular questionnaire dimensions.

Author/s (publication date)	Work	Relationship with child/ children	Sexual intercourse	Medical profession	Treatment	Infertility
Nojomi et al (2011)	39.57±9.96	34.85±13.9	44.83±10.76	36.13±12.65	45.36±14.93	50.55±15.23
Jones et al (2006)	25.9 ± 24.6	12.3±20.7	52.3±30.5	36 ± 29.1	52.4±28.5	62.1±30.9
Khong et al (2010)	32.9 ± 28.4	28.2 ± 28.5	44.1±33.2	20 ± 25.9	38.6 ± 29.5	51.1±33.3
Mengarda et al (2008)	43.4±23.5	49.3±24.8	56.1±23.5	35.4±18.8	50.5±22.7	64.8±22.1
Jones et al (2004)	43.4±26.8	35.2 ± 21.5	58.8±30.3	29.8±22.8	51.1±30.1	63.7±24.3
Jones et al (2001)	47.01±27.41	47.53±24.54	61.3±29.29	41.47±27.62	63.95±24.17	67.1±27.84
Nogueira-Silva et al (2015)	28.89±30.09	27.78±29	46.12±31.07	12.76±24.44	30.92±28.46	55.89±28.92

Also, in all included primary studies and in overall estimation of meta-analysis, infertility has the highest mean score and shows the most negative effect on the QoL. In return, the medical profession in 5 primary studies and relationship with children in 2 studies have the lowest mean scores and show the least negative effect on the QoL^{7-9,15,18,20,21}. In the overall estimation of meta-analysis, also, the medical profession has the lowest score.

CONCLUSIONS

Our findings showed that endometriosis affects all aspects of women's QoL negatively. Endometriosis has the most negative effect on the control and powerlessness among the core dimensions and infertility among the modular dimensions. Also, it has the least negative effect on the self-image among the core dimensions and medical profession among the modular dimensions. Therefore, early diagnosis and developing the effective treatment protocols are very important as they could prevent the reduction of women's QoL due to endometriosis.

AUTHORS' ROLE:

K. Ch contributed in study design, the search and quality assessment of primary studies and manuscript drafting, MAB contributed in the search and quality assessment of primary studies and manuscript drafting, MM contributed in the quality assessment of primary studies and data analysis, EB contributed in study design, the search and quality assessment of primary studies and manuscript drafting.

CONFLICT OF INTERESTS:

The Authors declare that they have no conflict of interests.

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