Endometriosis and COVID-19: Clinical Presentation and Quality of Life, a Systematic Review

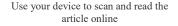
Poorya Davoodi^{1,2}, Delaram J. Ghadimi^{3,4}, Malihe Rezaei^{4,5,6}, Mohammad Amin Khazei Tabari^{7,8}, Aryan Shirani^{4,5}, Behnaz Nouri⁹, Noosha Samieefar^{4,5}, Meisam Akhlaghdoust^{2,10*}

- 1. Department of Molecular Medicine, University of Padua, Padua, Italy
- 2. USERN Office, Functional Neurosurgery Research Center, Shahid Beheshti University of Medical Sciences; Tehran, Iran
- 3. School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 4. USERN Office, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 5. Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 6. Tehran Heart Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
- 7. Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran
- 8. USERN Office, Mazandaran University of Medical Sciences, Sari, Iran
- 9. Department of Obstetrics and Gynecology, School of Medicine, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 10. Functional Neurosurgery Research Center, Shohada Tajrish Neurosurgical Comprehensive Center of Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Article Info

doi <u>10.30699/jogcr.8.4.315</u>

Received: 2022/04/16; Accepted: 2022/06/28; Published Online: 07 July 2023;





Corresponding Information: Meisam Akhlaghdoust, Functional Neurosurgery Research Center, Shohada Tajrish Neurosurgical Comprehensive Center of Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Email: <u>Akhlaghdoust@sbmu.ac.ir</u>

ABSTRACT

Background & Objective: Endometriosis, a common disease of the female reproductive system, could affect many aspects of women's lives. Along with many other diseases, COVID-19 has affected the diagnostic or treatment approaches towards endometriosis. This systematic review aims to investigate COVID-19 in endometriosis patients in terms of prognosis, diagnosis, treatment, and quality of life during the pandemic.

Materials & Methods: Relevant studies were identified through searching for endometriosis and COVID-19 in different databases, including PubMed, Medline, Scopus, and Web of Science, on 17 January 2022. Peer-reviewed published articles evaluating COVID-19 and endometriosis written in English were included.

Results: Out of 115 articles, 9 manuscripts met our criteria. Endometriosis does not intensify the risk of COVID-19 infection. However, COVID-19 has changed the health care of endometriosis patients.

Conclusion: COVID-19 has affected endometriosis patients' life in many aspects, including their job, lifestyle, and health care. Further studies are recommended to evaluate how the pandemic has affected endometriosis patients.

Keywords: Coronavirus disease, COVID-19, Endometriosis, Pandemic, SARS-CoV-2, Gynecology

Copyright © 2023, This is an original open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License which permits copy and redistribution of the material just in noncommercial usages with proper citation.

Introduction

Endometriosis is the ectopic presence of endometrial glands that causes chronic inflammation, pain, and infertility (1-3). Estimates show that approximately 10% of women of reproductive age have endometriosis, and most of them are symptomatic (4-7). The consequences of the disease can affect the patients' mental health, quality of life and interfere with interpersonal relationships and occupation (6, 8). The

standard diagnosis of endometriosis warrants surgical investigation and histopathologic confirmation, while clinical diagnosis is a challenge (3, 8).

After the Coronavirus disease (COVID-19) pandemic, medical care has experienced a dramatic change and reduced patient access on a global scale (9). Endometriosis patients have not been an exception, and

the diagnostic or treatment approaches towards them have altered (10). Besides, patients with chronic illnesses like endometriosis are experiencing mental health problems during social isolation (10-12). It is known that the COVID-19 imposes a greater risk of severe outcomes in patients with chronic and inflammatory diseases (12, 13), but it has not been clear whether it has worse outcomes in endometriosis patients or not, nor do we know how the pandemic has affected the mental health and quality of life in endometriosis patients (14).

Therefore, we conducted a systematic review to shed light on the impact of the COVID-19 pandemic on patients with endometriosis. Our objectives were to

determine COVID-19 prognosis in endometriosis patients, its influence on diagnosis and treatment, and patients' experience of their disease during the pandemic.

Methods

In accordance with "Preferred Reporting Project for Systematic Evaluation and Meta-Analysis" (PRISMA) guidelines (15), a systematic search on endometriosis and COVID-19 was conducted in different databases: PubMed/Medline, Scopus, and Web of Science on 17 January 2022. The search keywords are brought in the supplementary <u>Table 1</u>.

Database	Search string	Results
PubMed	("Endometriosis" [Mesh] OR "Endometriosis") AND "COVID" OR "COVID19" OR "COVID 19" OR "COVID-19" OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "Coronavirus Disease-2019" OR "Coronavirus Disease 2019" OR "Coronavirus infection-19" OR "Coronavirus infection 19" OR "Coronavirus infection-2019" OR "Coronavirus infection 2019" OR "Coronavirus-19" OR "Coronavirus 19" OR "Coronavirus]" OR "Coronavirus- 2019" OR "Coronavirus 2019" OR "Coronavirus2019" OR "Coronavirus- 2019" OR "Coronavirus 2019" OR "Coronavirus2019" OR "nCoV19" OR "nCoV 19" OR "nCoV-19" OR "nCoV2019" OR "nCoV 2019" OR "nCoV-2019" OR "2019nCoV" OR "2019 nCoV" OR "2019-nCoV" OR "2019 Novel Coronavirus" OR "2019-Novel Coronavirus 2019" OR "Novel Coronavirus-2019" OR "SARS-Coronavirus-2" OR "SARS Coronavirus-2" OR "SARS-Coronavirus 2" OR "severe acute respiratory syndrome coronavirus-2" OR "severe acute respiratory syndrome-coronavirus 2" OR "severe acute respiratory syndrome-coronavirus-2" OR "SARS-CoV-2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS-CoV2" OR "SARS-CoV-2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS-CoV2" OR "SARS-CoV-2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS-CoV2" OR "SARS-CoV-2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS-CoV2" OR "SARS CoV-2" OR "SARS CoV-2" OR "SARS CoV 2" OR "SARS-CoV2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS CoV 2" OR "SARS-CoV2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS CoV 2" OR "SARS CoV2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS CoV 2" OR "SARS CoV2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS CoV 2" OR "SARS CoV2" OR "COVID-19"[Mesh]	31
Scopus	 ("Endometriosis") AND ("COVID" OR "COVID19" OR "COVID 19" OR "COVID-19" OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "Coronavirus Disease-2019" OR "Coronavirus Disease 2019" OR "Coronavirus infection-19" OR "Coronavirus infection 19" OR "Coronavirus infection-2019" OR "Coronavirus infection 2019" OR "Coronavirus 19" OR "Coronavirus infection 2019" OR "Coronavirus19" OR "Coronavirus 19" OR "Coronavirus2019" OR "Coronavirus-2019" OR "Coronavirus 2019" OR "Coronavirus2019" OR "ncoV19" OR "ncoV-19" OR "ncoV-19" OR "ncoV-2019" OR "ncoV2019" OR "ncoV2019" OR "Coronavirus 2019" OR "2019nCoV" OR "2019 ncoV" OR "2019-ncoV" OR "2019 Novel Coronavirus" OR "2019-Novel Coronavirus 2019" OR "Novel Coronavirus-2019" OR "Novel Coronavirus-2019" OR "SARS-Coronavirus-2" OR "SARS Coronavirus 2" OR "SARS Coronavirus 2" OR "SARS-Coronavirus 2" OR "SARS-Cov-2" OR "SARS Cov-2" OR	49
WOS	All= ("COVID" OR "COVID19" OR "COVID 19" OR "COVID-19" OR "Coronavirus Disease-19" OR "Coronavirus Disease 19" OR "Coronavirus Disease- 2019" OR "Coronavirus Disease 2019" OR "Coronavirus infection-19" OR "Coronavirus infection 19" OR "Coronavirus infection-2019" OR "Coronavirus infection 2019" OR "Coronavirus-19" OR "Coronavirus 19" OR "Coronavirus19"	35

Database	Search string				
	OR "Coronavirus-2019" OR "Coronavirus 2019" OR "Coronavirus2019" OR				
	"nCoV19" OR "nCoV 19" OR "nCoV-19" OR "nCoV2019" OR "nCoV 2019" OR				
	"nCoV-2019" OR "2019nCoV" OR "2019 nCoV" OR "2019-nCoV" OR "2019				
	Novel Coronavirus" OR "2019-Novel Coronavirus" OR "Novel Coronavirus 19" OR				
	"Novel Coronavirus-19" OR "Novel Coronavirus 2019" OR "Novel Coronavirus-				
	2019" OR "SARS-Coronavirus-2" OR "SARS Coronavirus-2" OR "SARS-				
	Coronavirus 2" OR "SARS Coronavirus 2" OR "severe acute respiratory syndrome				
	coronavirus 2" OR "severe acute respiratory syndrome coronavirus-2" OR "severe				
	acute respiratory syndrome-coronavirus 2" OR "severe acute respiratory syndrome-				
	coronavirus-2" OR "SARS-CoV-2" OR "SARS CoV-2" OR "SARS-CoV 2" OR				
	"SARS-CoV2" OR "SARS CoV-2" OR "SARS-CoV 2" OR "SARS CoV 2" OR				
	"SARS CoV2") AND All= ("Endometriosis")				

After omitting duplicate results, two reviewers screened titles and abstracts; in case of disagreement, a shared decision was made by discussion.

The inclusion criteria were: 1) articles that their major aim was to evaluate COVID-19 and endometriosis in the following aspects: prognosis, treatment, diagnosis, and quality of life; 2) published articles in English; and 3) peer-reviewed published articles indexed in PubMed/Medline, Scopus and Web of Science.

Preprints, reviews, short communications, editorials, letters to the editor, comments, conference abstracts, conference papers, and articles that did not aim to study COVID-19 and endometriosis were excluded. Also, citations were searched for relevant articles. Finally, 10 articles were recruited and appraised, of them, 9 articles were considered except for one that was not in line with our objectives.

Two independent reviewers collected data from eligible articles, and a third one revised the data.

Results

Search results

A total of 115 articles were evaluated, and following the title screening process and removing duplication, 72 articles were included in this review. Finally, 9 articles met all the criteria. (See Fig. 1). The summary of the articles is provided in two categories: 1. Studies about the COVID-19 effect on diagnosis and treatment of endometriosis patients (see Table 2) and 2. Studies about the mental health and quality of life in these patients (see Table 3).

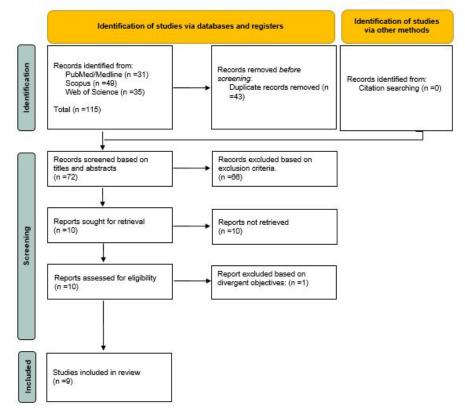


Figure. 1. PRISMA guidelines

Authors/ country	Study type/ participant number	Mean age	Highlights				
(16)	Internet-based survey collected 6,729	32.50 (Range: 18–73)	 20.3% had difficulty obtaining repeat prescriptions, 4.5% changed their hormone treatments, 7.0% changed painkillers, 3.4% stopped the hormone treatment, 6.6% stopped the painkiller treatments, and 64.6% reported no impact on the availability of the usual treatments. Cancelled/postponed gynecologist appointments, primary care appointments, surgeries, and fertility treatment procedures in 50.0%, 14.7%, 27.0%, and 12.0%, respectively 				
			15.9% increased the intake of over-the-counter painkillers ($p = 0.31$), and 15.9% added to the prescription-only pain drugs ($p = 0.91$).				
			45.30%, 40.50%, and 14.20% reported improvement, worsening and no change in pain intensity of dysmenorrhea, respectively (p=0.025).				
	web-based cross- sectional survey	32.05	No significant change was reported in other pain associated symptoms? with endometriosis (p>0.05)				
(17)	Retrospective 285	(Range: 27 – 36)	 43.6% (p<0.001) reported increase in frequent aware of pain, 37.2% (p = 0.09) experienced stress due to pain, 29.3% (p = 0.02) expressed pain as a distressing matter, and 30.0% (p<0.001) expressed pain as a threat. 				
			40.0% (p=0.08) reduction in possibility to relax despite the pain, and 43.9% (p = 0.09) no change in ability of pain management were reported.				
			36.6% (p = 0.001) decrease in verbalization of pain was reported.				
			41.8% and 36.8% enhancement of social and occupational functioning (p<0.001), respectively, and 29.9% enhancement of sexual functioning (p= 0.001) were reported.				
(18)	cross-sectional cohort study 181	35.00 (Range: 31.00 – 40.50)	32.4% enhancement in recreational functioning (p= 0.138), 36.7% worsening in family (p = 0.026), 19.2% improvement in self-care and life support (p > 0.05) were reported.				
			48.2% reported improvement of global physical impairment (p = 0.032). 27.07% (n = 49) and 8.83% (n = 16) reported increase and decrease in complaints, respectively.				
	case–control study 507 cases 520 controls		No significant difference in COVID-19 infection (3.2% vs. 3%; P = 0.942) was observed.				
			Higher frequency of asymptomatic infection (95.7% vs. 94.5%; P < 0.001) in control group was reported.				
(19)		29.08 ± 14.29	Higher frequency of fever (1.6% vs. 0%; $P = 0.004$) in the control was reported. However, no significant difference in the frequency of sore throat, stuffy nose, cough, dyspnea, headache, weakness, and myalgia was reported.				
			Anosmia and/or ageusia and eye problems did not differ between the two groups (all $p > 0.05$).				
			Higher frequency of rare symptoms in the case group (P < 0.001) and no difference in disease period (P = 0.694) was observed.				

 Table 2. Summary of the articles evaluating the diagnosis and treatment of endometriosis patients during the COVID-19 pandemic

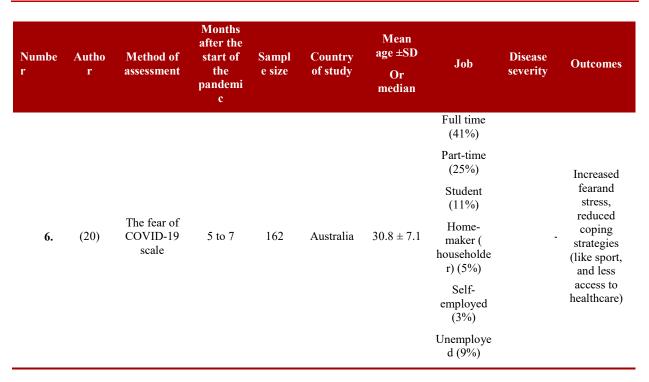
Authors/ country	Study type/ participant number	Mean age	Highlights		
	longitudinal examination 162		67% and 3% changed the physical appointments to telephone and video consultations appointments, respectively.		
			60% overall reported change in healthcare. 22% reported no impact on their daily functioning.		
(20)		30.8 ± 7.1 (18–50)	76% reported an impact on daily functioning.		
			12% reported the positive impact of limitation due to COVID-19, while 77% reported no change in their symptoms.		
			In 23% exacerbating of symptoms, stress, and decreased coping strategies were observed.		

Table 3. Summary of the articles about the mental health and quality of life of endometriosis patients during COVID-19

Numbe r	Autho r	Method of assessment	Months after the start of the pandemi c	Sampl e size	Country of study	Mean age ±SD Or median	Job	Disease severity	Outcomes
1.	(21)	Impact of COVID-19 on lifestyle and endometriosi s; Peri- traumatic distress inventory (PDI)	3	82	Puerto Rico	33.2±9.31	Full time (51.2%) Student (22%)	Mostly moderat e-to- severe	Increased job affection Increased peri- traumatic stress Changes in risk behaviors
2.	(22)	Endometrios is health profile 5 (EHP-5) The Italian version of Generalized Anxiety Disorder-7 (GAD-7) Spilberg State Trait Anxiety Inventory Y6 (STAI- Y6) Impact of Event Scale- Revised (IES-R)	5	468	Italy	38.8±7.7	Working from home (37.8%) Unemploye d (15%) Stopped working (18%) Went to work (28.6%)	Mostly moderat e to severe	Increased job affection Increased risk of PTSD Increased anxiety
3.	(23)	Self- administered online survey designed by	4	261	Turkey	34.19±5.9 0	-	Mild	Increased PTSD, depression, and anxiety; fear of

Numbe r	Autho r	Method of assessment	Months after the start of the pandemi c	Sampl e size	Country of study	Mean age ±SD Or median	Job	Disease severity	Outcomes
		Turkish endometriosi s and adenomyosis society							having endometriosi s-related problems and lack of gynecologic al help during the pandemic
									Postponed elective surgery
									Decreased quality of sexual activity
									Increased relaxing activities including breathing exercises, relaxing sleep, and meditations
									Increased attention to hand hygiene
4.	(16)	A survey designed by the University of Oxford in English and translated into French, German, Spanish, and Portuguese	5,6	6729	Global study (Europe, Oceania, North America, Latin America, and Caribbean)	32.5	-	-	Increased fear of being vulnerable to COVID-19; postponed appointment s and procedures; need for mental health support
5.	(18)	Fertility- related quality of life (FertiQol) Patient- centeredness of endometriosi s care questionnair e (ECQ)	5 to 10	330	Netherlan ds	33.00	-	Mostly moderat e to severe	Increased level of stress Decreased quality of life

Journal of Obstetrics, Gynecology and Cancer Research



Effect of COVID-19 on Endometriosis care

Among Nine studies, four studies evaluated alternations of the care of the endometriosis during social isolation or quarantine due to the COVID-19 pandemic. One online questionnaire-based survey reported a negative impact of the COVID-19 pandemic on the current or planned treatments of 80.7% [95% CI (79.7, 81.6)] among 6729 patients. Regarding the current treatment, difficulty obtaining repeated prescriptions, changing and/or stopping the hormone and painkiller were reported by participants. However, besides he impacts on planned care were more remarkable, with gynecologist appointments, primary care appointments, surgeries, and fertility treatment procedures were canceled or postponed (16). One study demonstrated that 60% of participants delineated that pandemic and related restrictions had changed their medical care, a range of unavailable or compromised providers and treatments, including fertility treatments, surgery/laparoscopy, medications, general practitioner and specialist appointment availability, and access to allied health, including pelvic physiotherapists (20). In another study, it has been demonstrated that 70% of patients with endometriosis mentioned that physical appointments were changed to telephone and video consultation appointments (18). Another study showed both the intake of over-the-counter pain medication and prescription-only pain medication was increased by 15.9% of 278 and 276 patients, respectively (p =0.31 and p = 0.91, respectively) (17).

Impact of COVID-19 pandemic on the pain intensity and cognition of Endometriosis

One of the nine studies assessed the alternations in pain experience and the influence of social isolation or quarantine on endometriosis patients during the COVID-19 pandemic. The study indicated that of 247 participants who answered the questions regarding the pain magnitude (measured by visual analogue scale) of dysmenorrhea, 45.30%, 40.50%, and 14.20% experienced improvement, worsening, and no change in pain, respectively. This result implies that the dysmenorrhea pain intensity decreased significantly during isolation or quarantine of COVID-19 in comparison with the pain intensity before quarantine (P = 0.025 < 0.05). However, the other pain associated with endometriosis, such as lower back pain, noncyclic pain, dyspareunia, dyschezia, and dysuria did not show a significant change (all P > 0.05). Of 280 patients, 43.6% (P<0.001) reported significantly more frequent awareness of pain or more pain hypervigilance, 37.2% (P = 0.09), 29.3% (P = 0.02) and 30.0% (P < 0.001) more participants experienced stress due to pain, pain as a disturbing event and pain as a threat, respectively. Nevertheless, the possibility to relax despite the pain was reduced in the 40.0% (P =0.08) of patients, and 43.9% (P = 0.09) of patients reported that the ability of pain management did not change. Verbalization of pain experience was significantly decreased in 36.6% (P = 0.001) of patients (17).

Impact of COVID-19 pandemic on the disability due to Endometriosis

Of Nine studies, two of them aimed to investigate the deterioration of functional disability-induced endometriosis caused by social isolation or quarantine during the COVID-19 pandemic. One study assessed the disability due to endometriosis-induced pain via using Pain Disability Index (PDI) during social isolation in respect of the period prior to isolation. The result of this survey showed a significant enhancement of social, occupational (P < 0.001), and sexual (P = 0.001) functioning. However, recreational functioning

did not exhibit a significant alternation. Taken together, the sum scores of the mentioned discretionary activities significantly improved (P = 0.001). But, the deterioration of family functioning was observed in the contrary direction (P = 0.026). Basic activity, including self-care and life support, remained unchanged during what (P = 0.218), and also, the global PDI score, which can reflect global physical impairment, demonstrated a significant improvement (improvement of 48.20% vs worsening of 40.90%, P = 0.032) (17). A study showed that 76% of patients reported the impact of the COVID-19 pandemic on daily functioning, most of them felt that life was now harder, including social exclusion, decreased work, and financial challenges. There were some reports indicating that the physiological function of these patients was affected in terms of anxiety and stress. Nevertheless, reduced function was not reported by all. Twenty women (12%) reported the positive outcomes from COVID-19 caused restrictions, including the convenience of telehealth, working from home, more opportunities to rest, and increased opportunities to obtain healthier habits (20).

Impact of COVID-19 pandemic on the social support of patients with Endometriosis

One survey reported that the empathy and social support received from the partner regarding pain experience showed no significant changes (both P > 0.05); whereas, the empathy and social support received from family and friends were significantly reduced during the social isolation (all P < 0.05) (17).

Concerns of endometriosis patients in COVID-19 pandemic

One study reported that more than half (54.2%) of patients had concerns of increasing their vulnerability to COVID-19 due to endometriosis (95% CI = 53.0, 55.4) (16). Another study reported that 35.9% of the 181 endometriosis patients experienced an increase in stress due to the delayed treatment during the pandemic (P < 0.001), and also 51.9% reported that they are able to overcome the changing health care system owing to the COVID-19 pandemic (P < 0.001) (18). One study demonstrated that higher fear of COVID-19 prophesied greater odds of reporting influenced healthcare, symptoms and daily functioning (odds ratio = 0.93, 95% confidence interval: 0.87-0.98; odds ratio = 0.88, 95% confidence interval: 0.82-0.95; odds ratio = 0.92, 95% confidence interval: 0.85–0.99, respectively) (20).

Impact of COVID-19 pandemic on the endometriosis-related complaints

Two studies investigated COVID-19 impacts on the symptoms of endometriosis. One study indicated that 33.1% of 181 patients (n = 60) reported their endometriosis-related complaints during COVID-19 had changed, in such 81.7% (n = 49) and 26.7% (n = 16) reported increase and decrease in complaints, respectively (**18**). Another study demonstrated that 77% of 162 participants reported that COVID-19 had

not affected their symptoms. Other patients (23%) reported worsening of symptoms such as pain, stress, and decreased withstanding strategies (for instance, sport and less access to healthcare) (20).

Endometriosis and susceptibility to COVID-19 infection

Only one study compared the COVID-19 characteristics between women with (n = 507) and without (n = 520) endometriosis. This manuscript showed there was no significant difference between patients with and without endometriosis with regard to COVID-19 infection (3.2% vs 3%; P = 0.942). Frequency of asymptomatic infection (95.7% vs. 94.5%; *P* < 0.001) and fever (1.6% vs. 0%; *P* = 0.004) were higher in the control group, while the frequency of sore throat, nasal congestion, cough, dyspnea, headache, weakness and myalgia, anosmia and/or ageusia and eye problems did not differ between two groups (all P > 0.05). However, other infrequent symptoms were more prevalent in the endometriosis group (P < 0.001). The average disease period was the same (14 days) in both groups (P = 0.694). Frequency of H1N1 vaccination, recent traveling to high-risk regions, social distancing, exposure to infected patients, frequency of implementing screening test, admission, and isolation due to COVID-19 had no significant difference between the two groups (P >0.05). But the case group significantly had a higher frequency of symptoms (P < 0.05) and H1N1 infection (P < 0.001). Also, this study indicated that close contact is the most significant risk factor for COVID-19 infection in both groups (r = 0.331; P < 0.001 in the case group and r = 0.244; P < 0.001 in the control group). Whereas the association between COVID-19 infection and other variables like social distancing, traveling, underlying diseases, thyroid diseases, and stage of endometriosis was not significant (P > 0.05) (19).

The impact of COVID-19 on endometriosis patients' mental health

There is a growing concern about the effect of the COVID-19 pandemic on the mental state of people worldwide.

A total of 8,032 people were studied in a report, with an average age of 20 to 50 years. All the studies were performed within the first year of the pandemic, ranging from 3 to 10 months after the outbreak. The study surveys were given to women from Puerto Rico, Italy, Turkey, the Netherlands, and Australia. Just one study was performed globally in Europe, Oceania, North America, Latin America, and the Caribbean (16). The disease severity was mostly in mild to moderate stages. Most of the participants were full-time workers, remote workers, students, and self-employed workers. The general effects of COVID-19 on patients with endometriosis are negative and positive effects. Negative effects include increased job affection, peritraumatic stress, job affection, Post-Traumatic Stress Disorder (PTSD), anxiety, depression, worry of having endometriosis-related problems, lack of gynecological help during the pandemic, fear of being vulnerable to COVID-19, and need for mental health support. Other negative effects include postponed elective surgery and appointments and a decrease in quality of sexual activity, quality of life, and coping strategies (such as sport and less access to healthcare). Positive effects include increased relaxing activities, including breathing exercises, relaxing sleep and meditation, and increased attention to hand hygiene (16, 18, 20-23).

The impact of COVID-19 on endometriosis patients' quality of life

According to the Ramos et al. study, many of the patients reported that their job status was affected. 17.3% of these patients had lost their jobs. On the other hand, healthy behaviors were also affected. 40% of the patients in this study reported a decreasing time in their exercise. 29.2% of these patients reported that their alcohol consumption had increased after the start of the pandemic. Fortunately, smoking was not increased. The Peri-traumatic Distress Inventory (PDI) score was increased significantly after the pandemic began (21). Growing concern about access to gynecologic care was reported in women in a study by Arena et al. The older age was demonstrated to be a risk factor for PTSD in this study. Up to 71.8% of the participants were diagnosed with severe anxiety. Although the pandemic affected the job status negatively, the authors declared that women who could leave home from work had beneath levels of PTSD (22). Yalçın Bahat and coworkers also showed that although endometriosis is associated with increased chronic stress, the COVID-19 pandemic clearly leads to psychological problems including PTSD, psychological distress, depression, and anxiety. Most of the patients were concerned about problems that may arise from endometriosis during the pandemic. While other studies showed an increase in postponed elective surgery, in this study, the surgery was mostly not postponed. It was also demonstrated that patients were becoming adapted to social distancing as well as paying more attention to hand hygiene. Eating habits were also reported to be healthier, and the diet became healthier than before the pandemic. Most of the patients believed that their sexual life was not highly affected by the pandemic (23). Demetriou *et al.* study was the only global study of all included studies. The patients in this study, mostly (over 50%), believed that their disease makes them more susceptible to COVID-19. Mental health was one of the highest priorities among the patients (20% of all) worldwide (16). A study in the Netherlands indicated that 35.9% of the patients with endometriosis experienced an increased stress level since the beginning of the pandemic. 35.9% of the patients experienced stress due to the delay in their treatment (21). In a study by Evans et al. it was demonstrated that just a quarter of the patients had no dysfunction in their lives, while the rest experienced harder lives. They reported that the patients missed

social communications, their jobs were affected, and they experienced financial problems. Other psychological disorders were discovered in these patients, including stress, fatigue, and other symptoms of anxiety and depression. Although the pandemic affected the endometriosis patients negatively, it had hidden benefits including having more rest, increased opportunities for healthier lifestyle in both nutritional habits and physical activity (20).

Discussion

Our study shows that endometriosis does not raise the risk of SARS-CoV-2 infection; However, Moazzami et al. indicated that endometriosis could increase the chance of symptomatic COVID-19 compared with patients without endometriosis. Of note, quarantine resulting from the COVID-19 pandemic has not induced exacerbation of pain in endometriosis patients (19). Nonsteroidal antiinflammatory drugs play a major role in relieving the pain of the patients. Actually, besides estrogen and progesterone compounds, they are first-line therapies for Endometriosis (24). Thus, providing these agents efficiently and making them available in this condition could be a rational reason for the concept that women with endometriosis could control their symptoms as much as before the pandemic. Furthermore, multiple studies signify the leading cause of painful symptoms in dysphoric mood and even depression of the patients (25, 26). This evidence warrants the meaningful role of symptom control of endometriosis in this situation. In the COVID-19 pandemic, virtual management is one of the alternative ways to manage patients. Particularly, studies show that endometriosis patients do more frequent virtual and telephone management. Although this type of management has general interests and obvious advantages in the pandemic, a reasonable issue of that is the lack of physical examination. As a consequence, we can suggest virtual and telephone visits and consultation for the patients, especially those with severe symptoms, just as a good alternative, not further (18, 27). It is worth noting that the COVID-19 pandemic has provided strategies known as teleworking, in which employees can work from their homes and perform their tasks without attendance at the workplace. A cross-sectional study indicated that women with endometriosis could have more efficient management of their symptoms, as working hours have been decreased, and teleworking and remote work have been prominent (28).

In such wise, one study reported improvement in dysmenorrhea pain intensity, which signifies the favor of teleworking. Despite the prevailing wisdom, Bahat *et al.* declared that many endometriosis patients do not consider their disease a risk factor for COVID-19. However, this study also showed that most of the patients were concerned about being more symptomatic during the pandemic. While considering this issue besides their lifestyle concerns, including sleep and sexual disturbances, it can be concluded that the pandemic negatively impacted mental health, which adversely affects the patients' peace of mind and quality of life (23). Thus, contrariety between studies about lifestyle changes is prominent, and further evaluation should be considered.

According to a recent study not included in our primary search, women with endometriosis are exposed to an increased risk of psychological and psychiatric disorders, including PTSD (24), which could be related to the fear of access to the health system services. However, medication availability seems to remain intact in the pandemic. However, we cannot deny disorganization and difficulties resulting from the postponement of visits, which make it troublesome for patients to plan (16). A rational factor for challenging the mental health of the patients seems to be thinking of COVID-19 exposure resulting from treatment procedures. Endometriosis patients for many causes, including infertility, may need surgical interventions; as shown in one of the studies, minimally invasive procedures are generally safe and could be performed without concern of increased risk of COVID-19 (29). This paper has a considerable limitation, mainly related to the narrow populations of the studies. Target populations were from developed and developing countries, where health services are easily accessible, and several strategies are implemented to minimize COVID-19 effects on the health system. On the other hand, undeveloped countries are more vulnerable to and have less compliance against the pandemic troubles because of less developed health care. This consideration highlights the need for further studies, especially in undeveloped countries, where data collection is more difficult.

Another limit to consider is the lack of valid documentation of the patients. Data gathering by online questionnaires has limitations, such as patients' honesty in terms of proven endometriosis and their medical history. Although, this type of survey resulted in the evaluation of more diverse samples around the world.

Conclusion

Our systematic review showed that the COVID-19 pandemic resulted in minor psychological problems for women with endometriosis, although the risk of being infected by COVID-19 was not increased. In addition, strategies obtained in the pandemic, including teleworking, remarkably provide some benefits in their lifestyle. As the effect of COVID-19 upon the severity of endometriosis symptoms remains controversial, further evaluations are needed to draw a definitive conclusion.

Competing interests

None declared.

Acknowledgments

None.

Contributions

P.D. participated in the search strategy, the research design of systematic review and the data analysis. D.G., M.R., M.K. and A.S. drafted the manuscript, and did articles screening. N.S. and B.N. critically revised the manuscript for important intellectual content, and approved the final version to be published. M.A. supervised the study, and revised the manuscript for important intellectual content. All authors have read and approved the manuscript.

Conflict of Interest

None.

References

- Denny E. Women's experience of endometriosis. J Adv Nurs. 2004;46(6):641-8.
 [DOI:10.1111/j.1365-2648.2004.03055.x] [PMID]
- Berkley KJ, Rapkin AJ, Papka RE. The pains of endometriosis. Science. 2005;308(5728):1587-9.
 [DOI:10.1126/science.1111445] [PMID]
- Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol. 2014;10(5):261-75. [DOI:10.1038/nrendo.2013.255] [PMID]
- Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. Best Pract Res Clin Obstet Gynaecol. 2004;

18(2):177-200. [DOI:10.1016/j.bpobgyn.2004.01.007] [PMID]

- Ashrafganjoei T, Bahman A, Noei Teymoordash S, Aminimoghaddam S, Ebrahimi A, Talayeh M. The Incidence of Ovarian Involvement in Endometrioid Endometrial Adenocarcinoma: A Retrospective Analysis. J Obstet Gynaecol Res. 2021;6(3):105-9.
 [DOI:10.30699/jogcr.6.3.105]
- Soliman AM, Coyne KS, Zaiser E, Castelli-Haley J, Fuldeore MJ. The burden of endometriosis symptoms on health-related quality of life in women in the United States: a cross-sectional study. J Psychosom Obstet Gynaecol. 2017;38(4):238-48. [DOI:10.1080/0167482X.2017.1289512] [PMID]

- Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet. 2010;27(8):441-7. [DOI:10.1007/s10815-010-9436-1] [PMID] [PMCID]
- Rowe H, Quinlivan J. Let's not forget endometriosis and infertility amid the covid-19 crisis. J Psychosom Obstet Gynaecol. 2020;41(2):83-5.
 [DOI:10.1080/0167482X.2020.1757200] [PMID]
- Barach P, Fisher SD, Adams MJ, Burstein GR, Brophy PD, Kuo DZ, et al. Disruption of healthcare: Will the COVID pandemic worsen non-COVID outcomes and disease outbreaks? Prog Pediatr Cardiol. 2020;59:101254. [PMID] [PMCID] [DOI:10.1016/j.ppedcard.2020.101254]
- Leonardi M, Horne AW, Vincent K, Sinclair J, Sherman KA, Ciccia D, et al. Self-management strategies to consider to combat endometriosis symptoms during the COVID-19 pandemic. Hum Reprod Open. 2020;2020(2):hoaa028.
 [DOI:10.1093/hropen/hoaa028] [PMID] [PMCID]
- Chudasama YV, Gillies CL, Zaccardi F, Coles B, Davies MJ, Seidu S, et al. Impact of COVID-19 on routine care for chronic diseases: A global survey of views from healthcare professionals. Diabetes Metab Syndr. 2020;14(5):965-7. [PMID] [PMCID] [DOI:10.1016/j.dsx.2020.06.042]
- Sayeed A, Kundu S, Al Banna MH, Christopher E, Hasan MT, Rasheda Begum M, et al. Mental health outcomes of adults with comorbidity and chronic diseases during the COVID-19 pandemic: a matched case-control study. Psychiatr Danub. 2020;32(3-4):491-8. [DOI:10.31234/osf.io/qh6b5]
- Al Mutair A, Al Mutairi A, Alhumaid S, Maaz Abdullah S, Zia Zaidi AR, Rabaan AA, et al. Examining and investigating the impact of demographic characteristics and chronic diseases on mortality of COVID-19: Retrospective study. PLoS One. 2021;16(9):e0257131. [PMCID] [DOI:10.1371/journal.pone.0257131] [PMID]
- Leonardi M, Horne AW, Armour M, Missmer SA, Roman H, Rombauts L, et al. Endometriosis and the coronavirus (COVID-19) pandemic: clinical advice and future considerations. Front Reprod Health. 2020;2:5. [DOI:10.3389/frph.2020.00005] [PMID] [PMCID]
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264-9, w64.
 [DOI:10.7326/0003-4819-151-4-200908180-00135] [PMID]
- Demetriou L, Cox E, Lunde CE, Becker CM, Invitti AL, Martínez-Burgo B, et al. The global impact of COVID-19 on the care of people with endometriosis. Front Glob Women Health. 2021:

65. [DOI:10.3389/fgwh.2021.662732] [PMID] [PMCID]

- Schwab R, Anić K, Stewen K, Schmidt MW, Kalb SR, Kottmann T, et al. Pain experience and social support of endometriosis patients during the COVID-19 pandemic in Germany-Results of a web-based cross-sectional survey. PLoS One. 2021; 16(8):e0256433. [PMID] [PMCID] [DOI:10.1371/journal.pone.0256433]
- Rosielle K, Bergwerff J, Schreurs AMF, Knijnenburg J, De Bie B, Maas JWM, et al. The impact of the COVID-19 pandemic on infertility patients and endometriosis patients in the Netherlands. Reprod Biomed Online. 2021;43(4): 747-55.[DOI:10.1016/j.rbmo.2021.06.001][PMID] [PMCID]
- Moazzami B, Chaichian S, Samie S, Zolbin MM, Jesmi F, Akhlaghdoust M, et al. Does endometriosis increase susceptibility to COVID-19 infections? A case-control study in women of reproductive age. BMC Women's Health. 2021; 21(1):119. [DOI:10.1186/s12905-021-01270-z] [PMID] [PMCID]
- Evans S, Dowding C, Druitt M, Mikocka-Walus A. "I'm in iso all the time anyway": A mixed methods study on the impact of COVID-19 on women with endometriosis. J Psychosom Res. 2021;146: 110508. [DOI:10.1016/j.jpsychores.2021.110508] [PMID] [PMCID]
- Ramos-Echevarría PM, Soto-Soto DM, Torres-Reverón A, Appleyard CB, Akkawi T, Barros-Cartagena BD, et al. Impact of the early COVID-19 era on endometriosis patients: Symptoms, stress, and access to care. J Endometr Pelvic Pain Disord. 2021;13(2):111-21. [DOI:10.1177/22840265211009634]
- Arena A, Orsini B, Degli Esposti E, Raimondo D, Lenzi J, Verrelli L, et al. Effects of the SARS-CoV-2 pandemic on women affected by endometriosis: a large cross-sectional online survey. Ann Med. 2021;53(1):1924-34. [PMID] [PMCID] [DOI:10.1080/07853890.2021.1991589]
- Yalçın Bahat P, Kaya C, Selçuki NFT, Polat İ, Usta T, Oral E. The COVID-19 pandemic and patients with endometriosis: A survey-based study conducted in Turkey. Int J Gynaecol Obstet. 2020; 151(2):249-52. [DOI:10.1002/ijgo.13339] [PMID] [PMCID]
- 24. Ferrero S, Barra F, Leone Roberti Maggiore U. Current and Emerging Therapeutics for the Management of Endometriosis. Drugs. 2018; 78(10):995-1012. [PMID] [DOI:10.1007/s40265-018-0928-0]
- 25. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature

review. Arch Intern Med. 2003;163(20):2433-45. [DOI:10.1001/archinte.163.20.2433] [PMID]

- 26. van Barneveld E, Manders J, van Osch FHM, van Poll M, Visser L, van Hanegem N, et al. Depression, anxiety, and correlating factors in endometriosis: a systematic review and metaanalysis. J Womens Health. 2022;31(2):219-30. [DOI:10.1089/jwh.2021.0021] [PMID]
- Nicolás I, Martínez-Zamora MÁ, Gracia M, Feixas G, Rius M, Carmona F. Impact of SARS-COV2 pandemic on patients with endometriosis and their health care. J Womens Health. 2022;31(4):480-6.
 [DOI:10.1089/jwh.2021.0323] [PMID]
- Armour M, Ciccia D, Stoikos C, Wardle J. Endometriosis and the workplace: Lessons from Australia's response to COVID-19. Aust N Z J Obstet Gynaecol. 2022;62(1):164-7.
 [DOI:10.1111/ajo.13458] [PMID] [PMCID]
- Crispi CP, de Almeida Nogueira E, Balthar PC, Guerra CGS, de Freitas Fonseca M. Endometriosis Surgery during the First Wave of the COVID-19 Pandemic: A Brazilian Single Institution Experience. Case Rep Obstet Gynecol. 2021;2021: 5040873. [DOI:10.1155/2021/5040873] [PMID] [PMCID]

How to Cite This Article:

Davoodi, P., J. Ghadimi, D., Rezaei, M., Khazei Tabari, M. A., Shirani, A., Nouri, B., et al. Endometriosis and COVID-19: Clinical Presentation and Quality of Life, a Systematic Review. J Obstet Gynecol Cancer Res. 2023; 8(4):315-26.

Download citation:

<u>RIS</u> | <u>EndNote</u> | <u>Mendeley</u> |<u>BibTeX</u> |