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Incidence of Endometriosis in Symptomatic and Asymptomatic Cases of Primary Infertility in Tanta University Hospital

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Endometriosis is the presence of endometrial-like tissue outside the uterus, which induces a chronic, inflammatory reaction. Some women with endometriosis experience painful symptoms and/or infertility, others have no symptoms at all. The aim of this study was to detect the incidence of endometriosis among symptomatic and asymptomatic cases of primary infertility in Tanta University Hospital over one year.
Methods: This prospective observational study was conducted on 50 females aged between 20 and 35 years old, with unexplained infertility, symptoms of endometriosis and infertility for 1 or more years. Patients were divided into two equal groups: group (1): cases with unexplained infertility for 1 year or more and group (2): cases with symptoms of primary infertility and endometriosis for 1 year or more. Patients were subjected to the following: meticulous history taking (personal, obstetric and menstrual history, history of present illness, past history 'medical and surgical'), thorough clinical examination, routine laboratory investigations, imaging techniques (ultrasound and HSG) and laparoscopy for diagnosis of possible presence of endometriosis.
Results: Endometrioma size was significantly higher in group 2 compared to group 1 (P value = 0.020). Stage 1 of endometriosis was significantly lower in group 2 compared to group 1 and Stage 2, 3 and 4 of endometriosis were significantly higher in group 2 compared to group 1 (P value =

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0.04). Dysmenorrhea of endometriosis after treatment were significantly higher in group 2 compared to group 1(P value <0.001). Chronic pelvic pain was significantly higher in group 1 compared to group 2 (P value <0.001).
Conclusions: The presence of dysmenorrhea, dyspareunia, pelvic pain, infertility, and clinical signs of cul-de-sac tenderness raise the suspicion of endometriosis in infertility patients.

Keywords: Endometriosis; symptomatic primary infertility; asymptomatic primary infertility.

1. INTRODUCTION

Endometriosis is a chronic inflammatory reaction caused by the existence of endometrial-like tissue outside the uterus. Some women with endometriosis have painful symptoms and/or infertility, while others have none at all [1].

Infertility is defined as the inability to conceive after one year of unprotected intercourse (independent of etiology). This disease affects about 10-15% of reproductive-aged people [1].

Although the exact cause of endometriosis is unknown, various theories have been proposed, including retrograde menstruation, altered immunity, coelomic metaplasia, and metastatic spread. Newer study also suggests that the disease has stem cell and genetic origins [2]. The exact location, extent, and depth of endometriosis implants, as well as the existence and severity of scar tissue and the presence and size of endometrial implants in the ovaries, are used to classify endometriosis into one of four stages (I-minimal, II-mild, III-moderate, and IV-severe). The majority of cases of endometriosis are classed as minimal or mild, meaning there are just minor scarring and superficial implants. Cysts and more extensive scarring are common side effects of moderate and severe endometriosis. The severity of endometriosis symptoms is unrelated to the degree of awomn experiences [2]. Endometriosis is said to be responsible for one third of infertility cases, however up to 70% of women with mild to moderate endometriosis are still capable of conceiving [3].

Endometriosis can lead to infertility by adhesions among ovaries, uterus and fallopian tubes impede the transfer of the egg to the fallopian tube, ovarian implants prevent release of the ova, decrease in the number and quality of healthy eggs and hyperestrogenemia [3].

Symptoms of endometriosis are pain, which can be: pelvic pain, severe menstrual cramps [4], low backache 1 or 2 days before the start of the menstrual period (or earlier), pain during sexual intercourse (dyspareunia), rectal pain (dyschezia), pain during bowel movements, infertility may be the only sign that you have endometriosis and abnormal bleeding [4].

On examination, endometriosis is indicated by pelvic soreness, a fixed retroverted uterus, tender utero-sacral ligaments, or swollen ovaries. If deeply infiltrating nodules are discovered on the utero-sacral ligaments or in the pouch of Douglas, and/or visible lesions can be seen in the vagina or on the cervix, the diagnosis is more certain [5]. The aim of this study was to detect the incidence of endometriosis among symptomatic and asymptomatic cases of primary infertility in Tanta University Hospital over one year.

2. PATIENTS AND METHODS

This prospective observational study was conducted on 50 females aged between 20 and 35 years old, with unexplained infertility for 1 or more years and symptoms of endometriosis and infertility for 1 or more years.

Written informed consent was obtained from all participants after full explanation of the technique and potential side effects following the guidelines of the ethical committee.

Exclusion criteria were female more than 35 or less than 20 years old, female with infertility less than 1-year, male factor of infertility, cases of secondary infertility, cases with irregular sexual life, ovulatory causes of infertility, cases with congenital anomalies and hostile cervical mucous.

Patients were divided into two equal groups: group (1): cases with unexplained infertility for 1 year or more and group (2): cases with symptoms of primary infertility and endometriosis for 1 year or more.

All patients were subjected to: meticulous history taking [personal history, obstetric history,

menstrual history, history of present illness, past history 'medical and surgical'], thorough clinical examination, [vitals, appearance, regional, abdominal, gynaecological], routine investigation [complete blood picture, coagulation profile, fasting blood glucose, liver enzymes, urea and creatinine, FSH, LH, AMH, PRL, TSH, Ca125, semen analysis, post coital test], imaging techniques [ultrasound and HSG], laparoscopy for diagnosis of possible presence of endometriosis, sample was taken from suspicious lesion [vesicles, endometriosis patches, chocolet cyst], then treated by fulguration electrocautery, or excision, and histopathology of any suspicious lesion taken by laproscope.

2.1 Statistical Analysis

For statistical data analysis, IBM-SPSS, version 24 (IBM-Corporation, Chicago, USA; August 2017) was utilised. The mean, standard deviation (SD), number, and percentage were used to represent the data. For quantitative data, the mean and standard deviation were employed as descriptive values. The student t test was used to compare the means of two groups, and the one-way analysis of variance (ANOVA) test has been used to compare the means of more than two groups; the individual p values between each two groups were calculated using the LSD post HOC test. For non-parametric data, Mann-Whitney and Kruskal-Wallis tests were employed instead of the student t test and ANOVA to compare medians rather than means between two or more groups. For non-parametric data, the Pearson Chi square test was employed instead of the Fisher's exact test to compare percentages of qualitative variables. To compare two quantitative variables, the Pearson correlation test was performed. The level of significance (P-value) for all of these tests is $P < 0.05$.

3. RESULTS

There was no significant difference between both groups regarding age, age of menarche, BMI, duration of infertility, cycle length and history Table 1.

Table 2 shows that there was no significant difference between both groups regarding laboratory investigations and pathological examination.

Regarding pelvic pain symptoms, no symptoms and chronic pelvic pain were significantly higher in group 1 compared to group 2 and dysmenorrhea and dysmenorrhe, Dyspareunia pain were significantly lower in group 1 compared to group 2 (P value <0.001). Regarding TVU, cysts and endometriotic lesion were significantly lower in group 1 compared to group 2 and normal finding was significantly higher in group 1 compared to group 2 (P value <0.001). Regarding HSG, adhesions was significantly lower in group 1 compared to group 2 and normal was significantly higher in group 1 compared to group 2 (P value <0.001) Table 3.

Table 1. Comparison between the two studied groups according to age, age of menarche, BMI, duration of infertility, cycle length, previous oral contraception use, family history of endometriosis, previous gynecological surgery and menstrual disturbances

		Group 1 (n = 25)	Group 2 (n = 25)	T test	P value
Age		26.88±4.456	25.57±5.43	0.063	0.950
Age of menarche		13.61±0.986	12.72±0.922	0.893	0.376
BMI		27.40±0.912	26.77±0.957	0.756	0.453
Duration of infertility (years)		2.96±1.25	2.88±1.37	0.155	0.877
Cycle length (21-35 days)		26.52±5.08	27.28±4.17	0.751	0.456
Previous oral contraception use		14 (56%)	15 (60%)	0.082	0.774
Family history of endometriosis		8 (32%)	10 (40%)	0.347	0.556
Previous gynecological surgery		6 (24%)	8 (32%)	0.397	0.529
Menstrual disturbances	Amenorrhoea	5 (20%)	5 (20%)	1.451	0.683
	Amenorrhoea, pain	3 (12%)	1 (4%)		
	Oligomenorrhoea	11 (44%)	14 (56%)		
	Oligomenorrhoea, hirsutism	6 (24%)	5 (20%)		

Data are presented as mean ± SD or frequency (%), BMI: Body mass index

Table 2. Comparison between the two studied groups according to laboratory investigations and pathological examination

	Group 1 (n = 25)	Group 2 (n = 25)	P value
AMH	2.056±0.6378	2.008±0.5480	0.793
LH (mIU/ml)	9.896±2.2369	8.836±2.3088	0.926
FSH (mIU/ml)	4.8912±1.262	4.122±1.112	0.789
PRL (ng/ml)	4.512±1.1421	4.112±1.001	0.971
TSH (mIU/ml)	3.93±0.430	4.05±0.358	0.831
FT3 (pg/ml)	3.124±0.652	2.99±0.696	0.512
FT4 (ng/dl)	1.382±0.72119	1.538±0.760	0.788
Serum testosterone (ng/ml)	28.22±4.7633	27.056±4.7194	0.390
Fasting serum insulin (uIU/ml)	19.036±2.0031	18.556±2.4614	0.453
Fasting sugar (mg/dl)	98.280±9.7447	96.760±10.3653	0.596
CA125	46.040±4.9622	47.400±5.6726	0.793
Lesion of endometriosis	7 (70%)	13 (65%)	0.606
Lesion of other pathology	3 (30%)	7 (35%)	0.844
Simple cyst	1 (33.3%)	4 (57.1%)	
Hemorragic cyst	2 (66.6%)	2 (28.5%)	
Benign tumor	0 (0%)	1 (14.2%)	

AMH: Anti-Mullerian hormone, LH: luteinizing hormone, FSH: follicle-stimulating hormone, PRL: prolactin, TSH: thyroid stimulating hormone, fT3: free triiodothyronine, fT4: free thyroxine, CA125: cancer antigen 125

Table 3. Comparison between the two studied groups according to pelvic pain symptoms, TVU and HSG

		Group		Chi square	P value
		1	**2**	50.000	**<0.001***
Pelvic pain symptoms	No symptoms	8 (32.0%)	0 (0.0%)		
	Chronic pelvic pain	8 (32.0%)	7 (28.0%)		
	Chronic pelvic pain, Dysmenorrhea	5 (20.0%)	5 (20.0%)		
	Dysmenorrhea	1 (4.0%)	6 (24.0%)		
	Dysmenorrhe, Dyspareunia	3 (12.0%)	7 (28.0%)		
TVU	Cysts	2 (8.0%)	7 (28.0%)	14.561	<**0.001***
	Endometriotic lesion	2 (8.0%)	8 (32.0%)		
	Normal finding	21 (84.0%)	10 (40.0%)		
HSG	Adhesions	2 (8.0%)	14 (56.0%)	13.235	<**0.001***
	Normal	23 (92.0%)	11 (44.0%)		

**: significant as P value ≤0.05, TVU: transvaginal ultrasound, HSG: hysterosalpingography*

Endometrioma size was significantly higher in group 2 compared to group 1 (P value = 0.020). Stage 1 of endometriosis was significantly lower in group 2 compared to group 1 and Stage 2, 3 and 4 of endometriosis were significantly higher in group 2 compared to group 1 (P value = 0.04). Absence of deeply infiltrating endometriosis was significantly lower in group 2 compared to group 1 and presence of deeply infiltrating endometriosis was significantly higher in group 2 compared to group 1 (P value = 0.024). Total number of DIE lesions was significantly lower in group 2 compared to group 1 (P value = 0.037). Laparoscopically confirmed endometriosis, peritoneal superficial endometriosis, ovarian endometrioma isolated and anatomical distribution of DIE were insignificantly different between both groups Table 4.

Table 4. Comparison between the two studied groups according to endometriosis and DIE

		Group 1 (n = 25)	Group 2 (n = 25)	Chi square test	P value
Laparoscopically confirmed endometriosis	**No**	18 (72.0%)	12 (48.0%)	0.725	0.395
	Yes	7 (28.0%)	13 (52.0%)		
Endometrioma size (cm) Mean ± SD.		**(n =7)** 1.34 ± 0.66	**(n = 13)** 3.43 ± 0.56	1.624	**0.020***
Stages of endometriosis (rARM) classification)		**(n = 7)**	**(n = 13)**		
	1	5 (71.4%)	3 (23.1%)	27.600	**0.04***
	2	1 (14.3%)	2 (15.4%)		
	3	1 (14.3%)	5 (38.5%)		
	4	0 (0.0%)	3 (23.1%)		
Peritoneal superficial endometriosis	**No**	23 (92.0%)	20 (80.0%)	1.495	0.209
	Yes	2 (8.0%)	5 (20.0%)		
Ovarian endometrioma isolated	**No**	22 (88.0%)	19 (76.0%)	1.220	0.463
	Yes	3 (12.0%)	6 (24.0%)		
Deeply infiltrating endometriosis (DIE)		**(n =25)**	**(n =25)**		
	No	22 (88.0%)	15 (60.0%)	5.094	**0.024***
	Yes	3 (12.0%)	10 (40.0%)		
Total number of DIE lesions Mean ± SD.		**(n = 3)** 3.00 ± 0.707	**(n = 10)** 2.20 ± 0.92	2.402	**0.037***
Anatomical distribution of DIE		**(n = 3)**	**(n = 10)**		
	Uterosacral ligament	1 (33.3%)	2 (20.0%)	0.956	0.695
	Intestine, USL	2 (66.7%)	5 (50.0%)		
	Vagina, Bladder	0 (0%)	3 (30.0%)		

**: significant as P value ≤0.05, DIE: deeply infiltrating endometriosis, USL: Uterosacral ligament*

Regarding dysmenorrhea of endometriosis after treatment, no dysmonrrhea was significantly lower in group 2 compared to group 1 and little improvement less than 50%, moderate improvement of symptoms 50-60%, significant improvement of symptoms 70-80% and complete improvement of symptoms 90-100% were significantly higher in group 2 compared to group 1(P value <0.001). Pregnancy rate was insignificantly different between both groups Table 5.

4. DISCUSSION

Endometriosis is a gynecological enigma since it is difficult to diagnose and treat. Endometriosis is a benign disease in which endometrial-like tissue persists outside the uterine cavity. Pelvic structures are most commonly affected, but endometriosis can involve extrauterine organs as distant as the lung [6].

Furthermore Moghadam et al. found that the prevalence of infertility on all couples in Canada-2011 was 11.5% - 15.7% [7].

A meta-analysis study in Iran was conducted on 13 Iranian studies during 2003-2011 by Bentley et al. which reported the overall infertility prevalence 13.2% [8].

In our study, we found that among cases of unexplained infertility in group (1), 28 % had endometriosis and among cases of primary infertility in group (2), 52% had endometriosis (P= 0.395, chi = 0.725).

Similar to our results a retrospective study conducted among 372 cases by Mao et al, which demonstrates a very high incidence of endometriosis 48.33% [9].

In the opposite to our study, study of Khadawardi et al, found that 10.7% of cases had endometriosis which lower than our percentage [10].

In Egypt, another study by Kulkarni et al, conducted among 100 patients attending Menoufia University Hospital and subjected to diagnostic laparoscopy reported that 33% of

Table 5. Comparison between the two studied groups according to dysmenorrhea in endometriosis among 3 months after laparoscopy and pregnancy rate after laparoscopy

		Group 1 (n = 25)	Group 2 (n = 25)	Chi square	P value
Dysmenorrhea of endometriosis after treatment		**(n =18)**	**(n = 13)**		
	No dysmonrrhea	18 (100.0)	0 (0.0)	22.496	**<0.001***
	Little improvement less than 50%	0 (0.0)	3 (23.1)		
	Moderate improvement of symptoms 50-60%	0 (0.0)	2 (15.4)		
	Significant improvement of symptoms 70-80%	0 (0.0)	3 (23.1)		
	Complete improvement of symptoms 90-100%	0 (0.0)	5 (38.5)		
Pregnancy rate	**No**	15 (60.0)	17 (68.0)	0.347	0.556
	Yes	10 (40.0)	8 (32.0)		

**: significant as P value ≤0.05*

them had endometriosis [11]. Another study by Gad et al, conducted among 1285 women reported; the estimated point prevalence of endometriosis was 4.0% [12].

There was high significant difference between both groups regarding pelvic pain symptoms. Most prevalent symptoms for endometriosis in this study were had chronic pelvic pain (32% in group 1 and 28% in group 2), dysmenorrhea (20% in both groups), dysmenorrhea together with dyspareunia (12% in group 1 and 28% in group 2). However, 32% of cases in group (1) experienced no symptoms and only 0 % of group (2).

In line with our results, Minko et al. concluded that twenty-five percent of women experienced no symptoms while chronic pelvic pain, dysmenorrhea and dyspareunia were the most prevalent symptoms recorded in their study [13].

In the present study, there was high significant difference between groups regarding TVU.As we found in group (1), 8% of cases had cysts ,8% had endometriotic lesions and 84 % show normal finding. In group (2), 28% of cases had cysts, 32% had endometriotic lesions and 40% show normal finding.

In Egypt, a prospective study done in Obstetrics and Gynecology Department, Faculty of Medicine, Alexandria University in 2016 to evaluate the role of HSG in the prediction of endometriosis among 86 females with primary infertility who undergo HSG 3 months before laparoscopy and the result is 36 cases (41.99%) show positive finding for endometriosis as adhesion and 50 cases (58.1%) show normal finding.

Furthermore, there was low significant difference between groups regarding laparoscopically confirmed endometriosis, peritoneal superficial endometriosis, and ovarian endometrioma isolated but high significant difference between them regarding endometrioma size, stages of endometriosis (rARM) classification.

In current study, there was significant difference between both groups regarding pregnancy rate. The pregnancy rate in our study was 40% in first group and 32% in second group who had endometriosis.

According to the findings, the pregnancy rate in Kulkarni et al's study was 36.36 percent, and the fertility rate (36.36 percent) was lower than in other studies. The likely cause is that infertile people have a greater prevalence of moderate to severe disease (75.75%), and many patients with severe disease are unable to undergo ART due to financial restrictions [11,14].

The fertility rate was 46 percent in a research by Sahu L et al. [15]. The latest advancements in surgical laparoscopy have revolutionised the way endometriosis with infertility is treated. Laparoscopic treatment includes identifying and removing lesions through cauterization, fulguration, or laser evaporation for minimal to mild disease, adhesiolysis, excision of deep lesions, cystectomy, drainage, and coagulation for moderate to severe ovarian endometriomas [11].

5. CONCLUSIONS

The Presence of dysmenorrhea, dyspareunia, pelvic pain, infertility, and clinical signs of cul-de-sac tenderness raise the suspicion of endometriosis in infertility patients. Laparoscopy remains the gold standard for diagnosis. As we found in our study that 28% of cases of unexplained infertility and 52% of cases of primary infertility had endometriosis.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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