

Epidemiology of Endometriosis in Tamil Nadu, India

T. Ramani Devi^{1,2*}, B. Kadalmani¹, C. Anchana Devi³

ABSTRACT

Endometriosis is an enigmatic disease of women of the reproductive age group. Pain and infertility are the main symptoms. This paper attempts to study the incidence of endometriosis among infertility patients undergoing laparoscopy. Following parameters such as age, SE status, body mass index (BMI), type of infertility, parity, symptoms, family history, menstrual history, medical history, ultrasound (USG) findings, stages of endometriosis, associated findings, and laparoscopy findings were analyzed. Incidence of endometriosis was higher between 26 and 35 years and at all ages stage 3 and stage 4 endometriosis were higher than stage 1 and stage 2. Endometriosis is more common in higher socio-economic class and in women with lower BMI and primary infertility. Among all the symptoms of endometriosis, dysmenorrhea is the most common and most important pointer towards the diagnosis of endometriosis. There is also higher incidence of family history among endometriosis patients. Menstrual cycles are invariably regular. Diagnosis of endometriosis is mainly through USG and rarely magnetic resonance imaging is performed to confirm the presence of endometriosis. In early stages of endometriosis, USG may not show any positive findings. USG can pick up endometriomas, deep infiltrative endometriosis, adenomyosis, and associated findings such as polycystic ovary syndrome, fibroids, and Mullerian anomalies. Laparoscopy is the gold standard in the diagnosis and treatment of endometriosis. Staging is done based on laparoscopy and simultaneously treatment is also carried out. Stage 1 and 2 patients underwent cauterization of the lesions. Advanced stages of endometriosis underwent cystectomy, adhesiolysis, and excision of the deep lesions and ultimately the pelvic anatomy is regained. Women were planned for further fertility treatment based on the staging of the disease.

Keywords: Body mass index, Endometriosis, Epidemiology, Laparoscopy, Ultrasound
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INTRODUCTION

Endometriosis is an elusive, enigmatic disease which is seen commonly among women of the reproductive age group. According to the American Society for Reproductive Medicine (ASRM), endometriosis is defined as chronic inflammatory disease which is estrogen-dependent, progesterone resistant, and needs life-long management plan. It is characterized by the presence of functional endometrial glands and stroma outside the uterine cavity. Thomas Cullen described endometriosis as a locally invasive disease.^[1] Endometriosis and Adenomyosis were discovered by Carl Rokitansky and the terminology was coined by John A. Sampson who was behind the theory of retrograde spill as an etiology for endometriosis.^[2] Endometriosis has varying phenotypes namely, superficial peritoneal (SUP) endometriosis, endometrioma, deep infiltrating endometriosis (DIE), and adenomyosis (endometriosis interna). Combinations of these phenotypes can occur. The presence of adenomyosis increases the incidence of chronic pelvic pain and infertility.^[3]

Symptoms observed are mainly pain and infertility. Pain could be classified as 7 Ds: dysmenorrhea, dyspareunia, dysuria, dyschezia, dysfunctional uterine bleeding, difficulty in conception, and diffuse abdominal pain, ultimately leading to severe depression. Extreme fatigability and disturbed bowel functions are also the features of endometriosis.^[4] 2–10% of the women may be asymptomatic.^[5] There is no correlation between the severity of the pain and the staging of the disease. Many a times, early lesions may cause severe pain because of the neuro angiogenesis. Isolated presence of endometrioma may be sometimes an incidental finding. DIE can lead to severe dyspareunia, dysuria, or dyschezia based on the location, namely, involvement of uterosacral, bladder, or rectum.

The origin of endometriosis has been explained by many theories, but none are definitive. They are Sampson's retrograde spill theory (1925), Ivan off Meyer's metaplastic theory (1924),

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Novak's hormonal theory of estrogen dependency and progesterone resistance (1931), Murphy's inflammatory and oxidative stress theory (1998), immunological theory by Semino (1995), suppression of apoptosis by Ferryman (1994) and Taniguchi (2011), genetic theory by Hadfield (1994), Albertsen HM (2013) and stem cell theory by Kato (2012) and Deane (2013).

Endometriosis can originate from environmental pollutants such as Polychlorobiphenyls, 2,3,7,8 Tetra-chloro dibenzo p-dioxin, Cadmium, and Dioxin causing endocrine disruption.

Incidence

National women's health information center from the US reported 10–20% women of reproductive age group and 2 million women in the UK do suffer from endometriosis. According to the study by P. Das Mahapatra of Endometriosis Society of India 2007, at least 26 million women of age between 18 and 35 are affected by endometriosis in

India.^[6,7] Study by the Endometriosis society of India in the year 2017 says more than 50 million women in India could have been affected. Still, it is only the tip of an iceberg. Current incidence may be even higher than the rate which was predicted already.

Approximately 176 million women in the world are affected by endometriosis according to World Endometriosis Research Foundation. Endometriosis affects roughly 10% of reproductive-age women and girls globally.^[8-10] Current incidence could be even beyond 190 million as per the WHO. Around 25–48% of women with infertility suffer from endometriosis.^[8,9] Similarly, 30–35% of women with endometriosis have infertility. Mean fecundity rate among patients with endometriosis is found to be 1–3% versus 20% per cycle in non-endometriotic patients. 60–70% of women with chronic pelvic pain have endometriosis. 3–5% of these endometriotic patients belong to the adolescent age group. It must be stressed that the diagnosis of endometriosis in adolescents remains a challenge and is almost inevitably delayed for several reasons and sometimes for a very long time. This diagnostic delay is very important because it allows endometriotic implants to progress towards the more destructive stages of the disease, with an often-irreversible impact upon the reproductive potential and the ovarian reserve of these young women.

A survey conducted by the World Endometriosis Society reported that the average time between the onset of pain and the final diagnosis of endometriosis is 9.3 years. Average delay of 6.7 years has been addressed in a study by Nnoaham *et al.*, 2011.^[11] Dun *et al.*, 2015 estimated that teenagers (average age 17.2 years) report a history of painful symptoms for a minimum period of 22.8 months and are seen by at least three specialists before arriving at an accurate diagnosis of endometriosis.^[12]

Endometriosis leads to economical burden to the patients which is in the form of loss of economy due to work loss and the amount spent towards medical, surgical, and infertility management. According to the Swedish study, the mean annual cost among all women suffering from endometriosis was 8,768 euros/woman. The direct healthcare cost of managing the disease was 4,282 euros, while the indirect cost was 4,486 euros/woman. Absence from work was reported by 32% of the women, while 36% reported reduced time at work because of pain due to endometriosis. These results confirm the substantial negative effect of endometriosis upon women's lives and their relatively high healthcare consumption.^[13] In countries where the medical support is provided by the government, it imposes burden to the government as well. Hence, we need to identify the patients with endometriosis earlier and treat them, so that they do not suffer from pain, infertility and progression of the lesion. Endometriosis is diagnosed in general by ultrasound (USG) or magnetic resonance imaging (MRI) which are non-invasive tests. Biomarkers like cancer antigen (CA)-125, CA 19-9, ILs, MMPs, HE-4, miRNA, neural elements in endometrium can pick up endometriosis, but none are considered for definitive diagnosis of endometriosis.

Laparoscopy is the gold standard in diagnosis and treatment of endometriosis. Staging of endometriosis can be done by applying laparoscopic findings to the revised ASRM (r-ASRM) score. Based on this, endometriosis is staged from Stage I to Stage IV as depicted in Figure 1.

In this study, we have tried to bring the incidence of endometriosis, age, staging, type of infertility, family history, and associated findings.

MATERIALS AND METHODS

This was a prospective study done at Ramakrishna Medical Centre LLP, which is a 40-bedded hospital at Tiruchirappalli, Tamil Nadu, India. The patients who underwent laparoscopy for infertility between January 2017 and December 2020 were included. Among those, patients who were found to have Endometriosis were separated giving an incidence of 35.9%. A total of 546 patients underwent laparoscopy, among which 196 were found to have Endometriosis ranging from Stage I to IV. Out of which 192 patients met the inclusion criteria. All the procedures were done by a single consultant.

Inclusion Criteria

- Age group: 20–40 years
- Both primary and secondary infertility
- Positive diagnosis for endometriosis of all Stages.

Exclusion Criteria

- Patients who underwent laparoscopy for other gynecological disorders
- Endometriosis patients over 40 years of age
- Not having fertility issues.

Following Parameters were Analyzed

- Age
- Socioeconomic status
- Body mass index (BMI)
- Primary/secondary infertility
- Parity
- Symptoms
- Family history of endometriosis
- Menstrual history
- Medical history
- USG findings
- Stage of endometriosis
- Associated findings– polycystic ovary syndrome (PCOS), fibroids, adenomyosis, and tubal diseases
- Laparoscopic findings based on revised American Fertility Society (rAFS) - Scoring and staging of endometriosis.

All these data were entered into SPSS Version 20.0. Categorical data were expressed in frequency (or) percentage. Chi-squared test and Fisher's Exact Test were performed to obtain the *P*-value.

RESULTS

546 patients with infertility were subjected to Diagnostic hystero-laparoscopy with chromotubation between January 2017 and December 2020. Among that, 196 patients were found to have Endometriosis of any stage giving an incidence of 35.9%. Mean age group was categorised into four groups.

The maximum incidence was observed in Group 26–30 years (46.35%) followed by 31–35 years (23.4%) and 20–25 years (19%). Beyond 35 years up to 40 years, only 13.02% were found to have endometriosis. Overall the incidence was high between 26 and 35 years (69.75%).

Even in women between 20 and 25 years 8/37 (21.62%) had stage I and II endometriosis and 29/37 (78.37%) had stage III and stage IV endometriosis. Women between 26

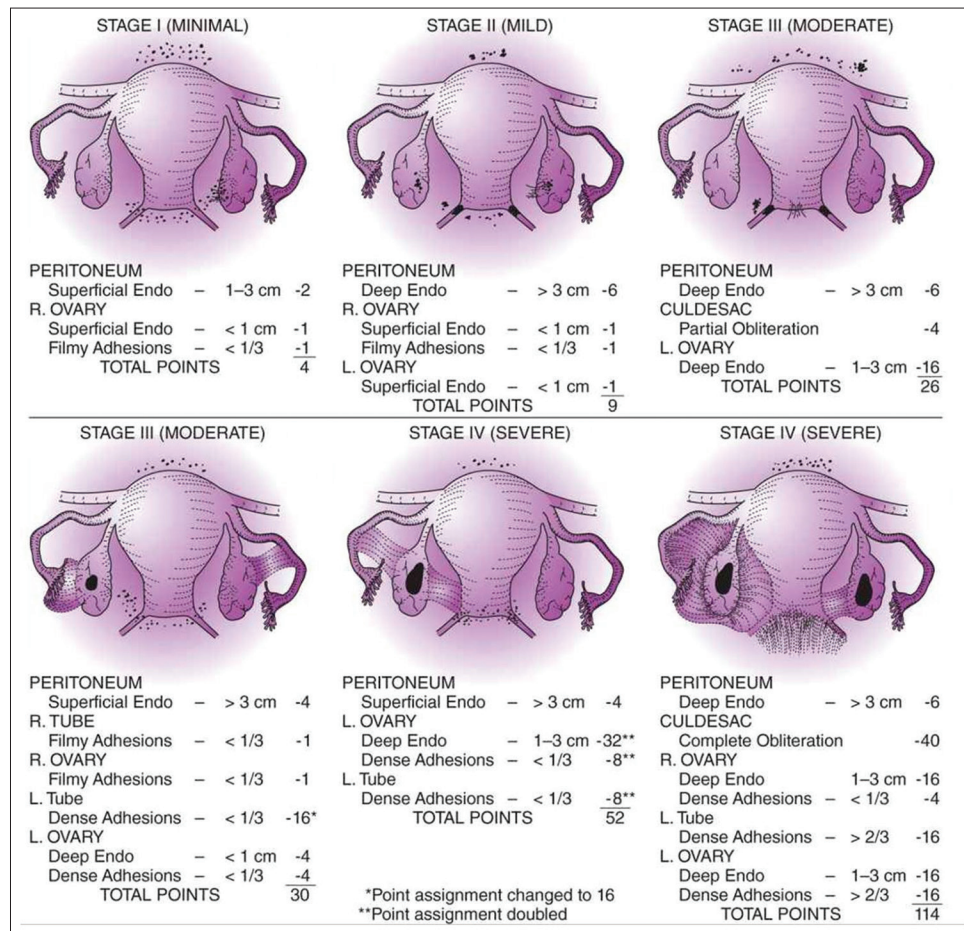


Figure 1: Stages of endometriosis. Source: <https://www.endometriosis-india.com/classification-of-endometriosis/>

and 30 years 23/86 (26.74%) had stage I and II endometriosis and 63/86 (73.26%) had stage III and stage IV endometriosis. Women between 31 and 35 years 14/45 (31.11%) had stage I and II endometriosis and 31/45 (68.9%) had stage III and stage IV endometriosis. Women between 36 and 40 years 3/24 (12.5%) had stage I and II endometriosis and 20/24 (83.33%) had stage III and stage IV endometriosis depicted in Figure 2. The inference from our previous study^[14] showed that among all ages, stage III and stage IV endometriosis were higher which was in contrast to the study by Mishra *et al.*,^[15] where Stage I and Stage II Endometriosis were predominant than Stage III and IV.

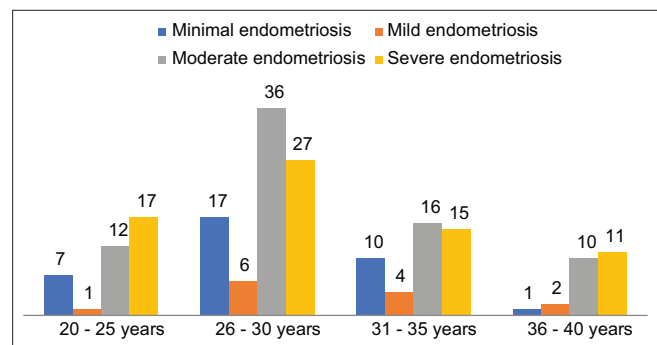


Figure 2: Age and stages of endometriosis

Incidence of Staging of Endometriosis in this Study

In our study, 48/192 (25%) of the patients had minimal to mild endometriosis (stage I and II). Moderate endometriosis (stage III) was seen in 74/192 (38.5%) and severe endometriosis (stage IV) was seen in 70/192 (36.5%) which is depicted in Figure 3.

Socioeconomic Status

Only 4% of the women included in this study had a family income of <Rs. 20000/pm. 76% of the women the family income was between Rs. 20000/pm and Rs. 50000/pm and 20% of the women had the family income of >Rs. 50000/pm which is depicted in Figure 4.

BMI

When BMI of the patients were studied, 82/192 (42.7%) were in normal weight and 82/192 (42.7%) were in over weight category. 15/192 (7.81%) patients were underweight. Only 13/192 (6.77%) patients were obese which shows that endometriosis is uncommon in obese individuals [Figure 5].

BMI and Staging of Endometriosis

For all stages of endometriosis highest incidence in seen among normal weight and overweight categories. In BMI <18 and more than 30 is found to be very low [Figure 6].

Parity

Out of 32 (17%) patients with secondary infertility 31 had abortions ranging between 1 and 4 and 1 patient had previous history of 8 abortions. 2 had ectopic pregnancies. There were 39 live babies of which 21 patients had 1 live baby and 17 had 2 live babies and 1 had previous intrauterine device. This study shows primary infertility and incidence of abortions were quite high among endometriosis patients [Figure 7].

Primary Infertility and Age Group

The incidence of primary infertility was observed in 128 (66.7%) patients among which, 28 were between the age group of 20 and 25 years, 67 were between 26 and 30 years, 23 were between 31 and 35 years,^[10] were between 36 and 40 years.

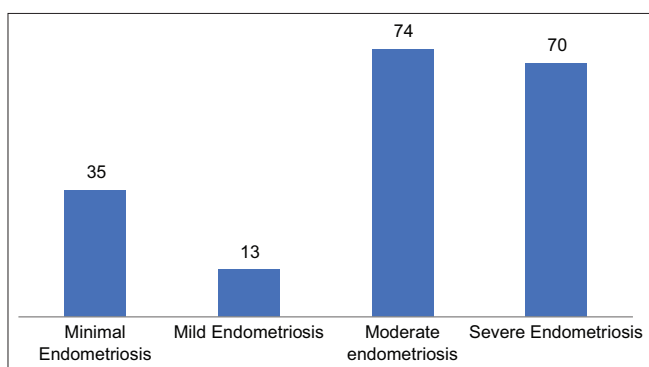


Figure 3: Stages of endometriosis

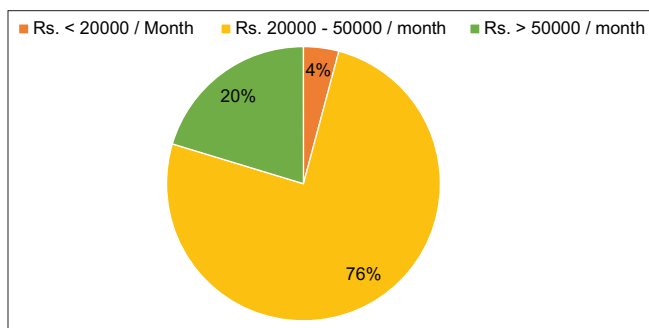


Figure 4: Socio economic status

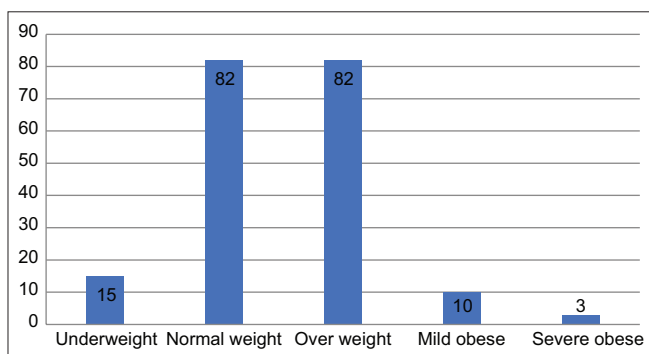


Figure 5: Body mass index of the respondents

Secondary Infertility and Age Group

The incidence of secondary infertility was observed in 32 (16.7%) patients among which, 6 were between the age group of 20 and 25 years, 10 were between 26 and 30 years, 14 were between 31 and 35 years, 2 were between 36 and 40 years. The incidence of primary infertility was seen 73% among (20–30 years) versus 50% among (20–30 years) of secondary infertility showing that higher incidence of primary infertility was seen among younger age group.

Percentage of Symptoms

Following symptoms were studied: dysmenorrhoea, dyspareunia, dysuria, dyschezia, A(D)UB, Diffuse abdominal pain and difficulty in conception. The symptoms seen were more than one in many patients. Single symptom was positive only in 17.7% of the patients, rest 82.3% had beyond two symptoms. Hence, patients having more than two symptoms suggestive of endometriosis should be screened for endometriosis, so that early diagnosis is possible and can be used as an initial screening test [Figure 8].

Symptoms

- Dysmenorrhea–136 (70.8%)
- Diffuse abdominal Pain–81 (42.2%)
- Dyspareunia–56 (29.2%)
- D(A)UB–50 (26%)
- Dysuria–45 (23.4%)
- Dyschezia–39 (20.3%).

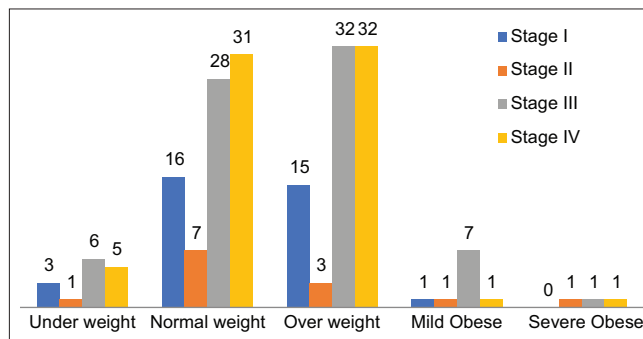


Figure 6: Relationship of body mass index with staging of endometriosis

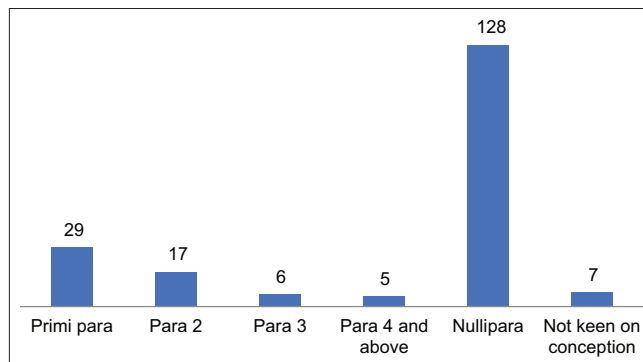


Figure 7: Parity of the respondents

Depression as a result of chronic pelvic pain and infertility are seen almost in 85% of the women in this study.

Among the symptoms, dysmenorrhoea had the highest incidence (70.8%) followed by diffuse abdominal pain (42.2%), and rest of symptoms were ranging between 20 and 30%. Asymptomatic patients were 26/192 (13.54%) and they have come for treatment of infertility alone [Figure 9]. Among 128 cases of primary infertility, minimal was seen in 29 (22.6%), Mild endometriosis in 8 (6.25%), Moderate endometriosis in 52 (40.6%) and Severe endometriosis in 39 (30.4%).

Among 32 cases of secondary infertility, minimal was seen in 6 (18.5%), Mild endometriosis in 2 (6.25%), Moderate endometriosis in 10 (31.25%) and Severe endometriosis in 14 (43.7%) [Figure 10].

In primary infertility moderate and severe endometriosis was seen in 71% and among the secondary infertility 72% of patients had moderate and severe endometriosis. In this study 3/4 of the women irrespective of whether primary or secondary had moderate to severe endometriosis.

Family History and Endometriosis

26/192 (13.5%) patients had family history of endometriosis. Most often the mother 14/26 (53.8%) or siblings 9/26 (34.61%) had endometriosis and 3/26 (11.53%) maternal aunts had endometriosis [Table 1].^[16]

Menstrual history

- Regular cycle-168/192 (87.5%)
- Irregular cycle-24/192(12.5%)

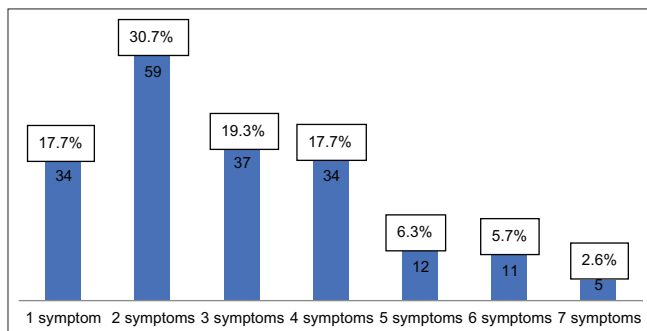


Figure 8: Percentage of symptoms

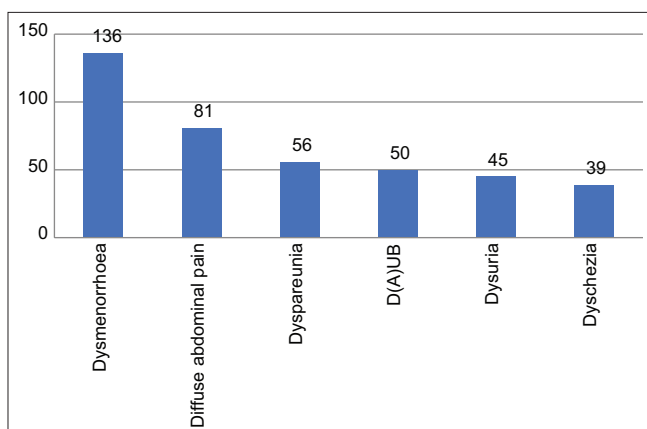


Figure 9: No. of symptoms considered for the study

Most of the patients had regular cycles. 12/24 women had associated PCOS which could be the reason for irregular cycles or it could be anovulation in rest of the patients.

Medical history

16% had hypothyroidism and 1-2% had diabetes and hypertension, majority of the women did not report any major medical complications [Figure 11].

USG Findings

All our patients had pre-operative evaluation of USG by Transvaginal (TV) sonography and MRI was rarely performed. Normal USG findings were reported in 48 (25%), Unilateral endometrioma were seen in 77 (40.1%), Bilateral endometrioma were seen in 67 (34.9%), Associated adenomyosis in 36/192 (18.75%), DIE in 46/192 (23.95%). 20 patients with unilateral endometrioma had associated DIE and 26 patients with bilateral endometrioma had associated DIE [Figure 12].

Associated Findings of USG

USG showed evidence of associated PCOS in 12 (6.25%) patients, fibroids in 5 (2.6%) patients and Mullerian anomalies in 6 (3.1%) patients. (Septate - 4, bicornuate -1 and didelphys uterus -1), Tubal disease in 27 (14.06%) cases [Figure 13].

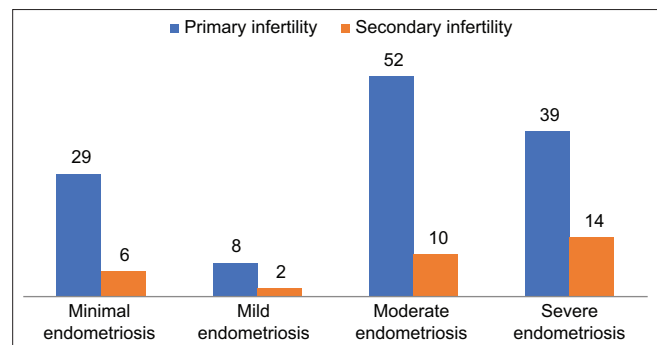


Figure 10: Infertility and staging of endometriosis

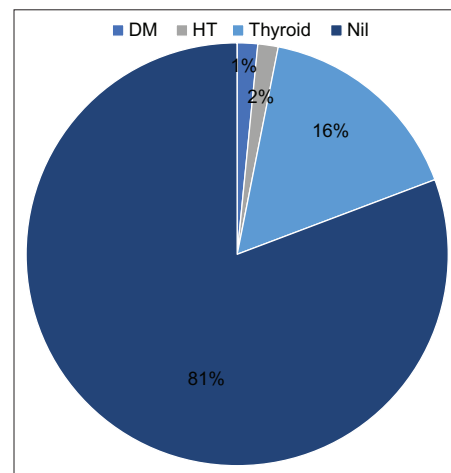


Figure 11: Associated medical complications of the respondents

Surgical Procedures Done

192/546 (35.16%) patients who underwent laparoscopy had any stage of endometriosis varying from stage I–IV. Stage I and II which included minimal and mild endometriosis underwent cauterisation, excision, adhesiolysis and pelvic anatomy was regained. Patients with Stage II and III endometriosis who had unilateral or bilateral endometrioma with dense pelvic adhesions underwent cystectomy and adhesiolysis. Chromotubation was done to assess the tubal patency in all patients. Additional myomectomy was done in needed cases. Adeno-myomectomy was deferred.

Pelvic anatomy and tubo-peritoneal relationship were normalized as far as possible. Adhesion preventing barriers were used as per the requirement. In patients with Mullerian anomaly especially septate uterus, septostomy was done along with cauterisation of endometriosis or cystectomy of endometrioma.

Post operatively all patients requiring infertility management were given 2 - 3 doses of GnRH Analogues. Stage I and stage II patients were treated with ovulation induction/timed intercourse or ovulation induction with intrauterine insemination (IUI). Stage

III and stage IV patients were treated with ovulation induction/ IUI/assisted reproductive technology (ART) depending upon the ovarian reserve. Associated male factor and tubal factor at any stage of endometriosis, patients were advised direct ART. Results of infertility treatment are beyond the per view of this article.

DISCUSSION

Endometriosis is a chronic debilitating illness which affects the quality of life in women by causing pain and infertility which becomes a social problem. There is often a diagnostic delay which may be up to 9 years. In this present study we have tried to analyse the following parameters: Age, socioeconomic status, primary/secondary infertility, parity, symptoms, family history, menstrual history, medical history, BMI, USG findings, laparoscopic findings based on rAFS - Scoring and staging of endometriosis and associated findings like PCOS, fibroids, adenomyosis and tubal diseases.

Incidence

Incidence among infertile patients in our series 192/546 (35.16%). In our previous study, the incidence was again found to be 34.2%.^[14,17] Study by Mishra *et al.* in the year 2014 reported as 48.3%^[15] and in 2017 the incidence was found to 54.98%.^[18] Valson *et al.*, in 2016 reported a very high prevalence of 73.33% of endometriosis among infertile women.^[19]

Age

Mean age in our study was 29.7 ± 5.08 years. In a study by Mishra *et al.*, 2017, the Mean age of was found to be 28.5 ± 4.2 years, which correlates with our study. Another study by Tomar *et al.*, 2017 also reported a similar mean age of incidence to be 27 ± 3.6 years.^[20]

Socioeconomic Status

The socioeconomic status of our patients were upper middle class and upper class. 4% of the patients had <Rs. 20,000/- of family income per month. 76% of the patients had Rs. 20,000/- –50,000/- of family income per month and 20% of the patients had >Rs. 50,000/- of family income per month. This shows endometriosis is likely to be more common in women of higher socio-economic group^[21] which may be due to delay in the age of marriage and fewer parity.

BMI

Endometriosis is more common among the non-obese category. Our study showed 7.81% incidence in underweight category, higher incidence of 42.07% among the normal weight and over weight category and there was only 6.7% incidence among obese women.^[22]

Study by Saha *et al.*, 2013 showed that there was inverse correlation of endometriosis and body weight. Nurses' health study II which included a cohort of 116,430 female nurses showed 5504 (4.72%) had a proven incidence of endometriosis, which shows there was a gradual reduction in the incidence of endometriosis as the BMI increased. The prevalence of endometriosis was very low in women with severe obesity.^[23]

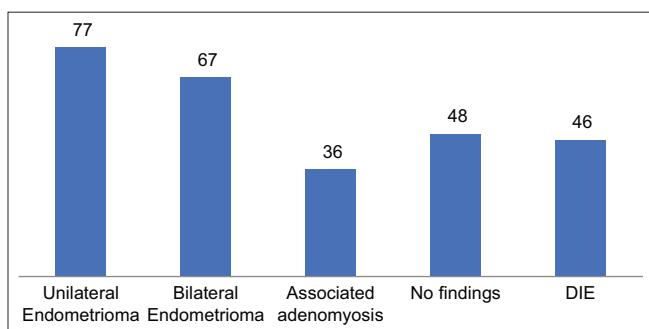


Figure 12: Ultrasonography findings of the respondents

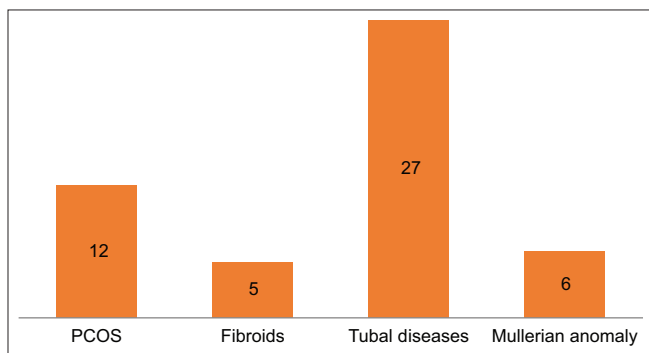


Figure 13: Associated Ultrasonography findings of the respondents

Table 1: Correlation between Family history and symptoms of the respondents

No. of Symptoms	Family history		Statistical inference
	Yes	No	
1 symptom	1	33	X ² =3.098 df=190 P<0.01 Significant
2 symptoms	5	54	
3 symptoms	5	32	
4 symptoms	9	25	
5 symptoms	1	11	
6 symptoms	4	7	
7 symptoms	1	4	
Total	26	166	

Saha *et al.*, 2017 study which included 28,822 women out of which 1228 (4.26%) had endometriosis. The odds ratio for overweight was observed as 1.48 and for obese women was 1.36 respectively.^[23] Meta analysis by Liu and Zhang *et al.*, 2017 suggested that higher BMI was associated with lower risk of endometriosis,^[24,25] whereas, Jenabi *et al.*, 2019 study showed underweight as a risk factor for endometriosis while obesity did not show any significant protective effect.^[26] A study in Korean population by Seo *et al.*, 2021 did not reveal any association between BMI and severity of disease.^[27] Similarly, Iranian study also showed women with endometriosis had lower BMI than controls. Hence, research should be focused on different anthropometric measures. Potential molecular and genetic connections are alternate methodologies to elucidate the complex relationship between obesity and endometriosis.^[28]

In association between symptoms and BMI, $P = 0.00001$ indicates that the variables are highly dependent on each other and there is a statistically significant association between both the factors, which implies that the BMI of the respondents strongly influence the symptomatic condition pertaining to Endometriosis [Table 2].

Primary/Secondary Infertility

The incidence of primary infertility was among 73% between 20 and 30 years and incidence of secondary infertility which was seen among 50% of patients between 20 and 30 years, showing that primary infertility was seen more in younger age group. In Mishra *et al.*, 2015 study 85.14% of patients had primary infertility and 14.85% had secondary infertility. In our own previous study, primary infertility was seen in 84.5% and secondary infertility was seen in 15.5%.^[29] Women with endometriosis had twofold increased risk of infertility. The incidence of primary infertility was 70%.^[30] A study by Tomar *et al.*, 2017 also reported 70% incidence of primary infertility and 30% of secondary infertility. As such 44.11% of patients with infertility have endometriosis.^[20]

The incidence of primary infertility is found to be more between the age of 26 and 30 years than that of secondary infertility. This is similar to the study by Vercellini *et al.*, 2014.^[31] Endometriosis among infertility was around 44.11%. The incidence according to Tsuji *et al.*, 2009 was 63%.^[32] There is high variation of the incidence of endometriosis among infertile women because of the lack of facilities for laparoscopy.

Meuleman *et al.*, 2008 reported 47% prevalence of endometriosis among infertile women.^[18] In 2017, a study by Mishra *et al.*, had reported 54.98% incidence of endometriosis among infertile women where as his previous study in 2014 reported 48.38%.^[15] Valson *et al.*, in 2016 reported an incidence of 73.3%.^[19]

Type of Infertility

The present study reports high incidence of primary infertility. There was high incidence of abortions (ranging between 1 and 8) in cases of secondary infertility in our study. In the previous study by Mishra *et al.*, 2017 and our own previous study, no details regarding the previous history of abortions were recorded.^[15]

The incidence of primary infertility is found to be more between the age of 26 and 30 years than 0000-00-00 0:00:00 AM that of secondary infertility. This is similar to the study by Vercellini *et al.*, 2014.^[31] According to Chapron *et al.*, 2019 the diagnosis of endometriosis could be by mere symptoms and clinical findings which helps in starting the treatment empirically with Progestins.^[33] The management plan depends upon the need of the patient. Pain can be managed only through medical management (COCs, Progestins, GnRH analogues, LNG-IUS, Aromatase inhibitors), failing which, surgery can be undertaken.

Patients with infertility in early stages of endometriosis may not be picked up by USG and most often these patients are treated as unexplained infertility. Management of these patients could be either by surgery or directly referred to ART, if they have associated male factor or tubal factor. Endometriosis fertility index (EFI) is one, which is derived from the history, age, previous pregnancy and laparoscopic findings based on r-AFS score.^[34] EFI has a score of 1–10. Higher the score, patients will have better spontaneous pregnancy outcome (0-4 or <4 may be advised ART, score of 5 and 6 can be offered OI with IUI or ART and they need counselling). Surgery for endometriosis improves spontaneous conception rate as well as reduces the pain to almost 60–70%. Still, the recurrence rate in the form of pain or lesion may be up to 20% at the end of 2 years and 40–50% at the end of 5 years.^[35]

Parity

128/192 (66.6%) were nullipara, 8/192 (4.16%) who were not keen on conception and the rest were secondary infertility with previous h/o missed miscarriage ranging from 1 to 4 with the maximum of 8.

This study investigated the relationship between the severity of endometriosis, using precise phenotypes, and the rate of miscarriage. We found that the rate of previous miscarriages were higher in all of the different phenotypes of the disease (SUP, ovarian endometrioma and DIE), although the rate was somewhat higher in patients with superficial endometriosis. Wheeler *et al.*, in 1983 reported that mild endometriosis was associated with a significantly higher proportion of miscarriages (49%) than moderate (25%) or severe (24%) forms of the disease.^[36] We put forward two hypotheses to explain this phenomenon: (i) early metabolic active lesions may display greater levels of molecular disorders, such as inflammation^[31] compared

Table 2: Correlation between symptoms and BMI

No. of Symptoms	BMI					Statistical inference
	Under weight	Normal weight	Over weight	Mild Obese	Severe obese	
1 symptom	3	11	20	0	0	$\chi^2=53.338$ df=24 $P<0.01$ Significant
2 symptoms	2	27	25	2	3	
3 symptoms	1	22	13	1	0	
4 symptoms	1	13	13	7	0	
5 symptoms	3	4	5	0	0	
6 symptoms	3	3	5	0	0	
7 symptoms	2	2	1	0	0	
	15	82	82	10	3	

BMI: Body mass index

with fibrotic lesions of advanced endometriosis^[37] or (ii) reproductive performance is impaired in women with severe endometriosis, leading to an overall decreased number of pregnancies and subsequent decreased miscarriage rate.^[38]

Symptoms

Symptoms can provide a clue to the diagnosis of endometriosis. Dysmenorrhoea was the most important presentation seen among 70.2%, followed by diffuse abdominal pain in 42.9%. Rest of symptoms ranged between 20 and 30%. Number of asymptomatic patients were 26/192 (13.54%) who came for treatment of infertility alone. Most of the patients had combination of dysmenorrhoea with diffuse abdominal pain. Dyspareunia, dyschezia and dysuria were seen more in severe endometriosis patients. Diffuse abdominal pain or chronic pelvic pain was found to be more associated in infertile women.

The commonest symptoms were seen in Tomar *et al.*, 2017 study was dysmenorrhoea 45.5% whereas, in our study it was up to 70%. AUB was seen in 21% in Tomar study, in our study it was 26%. The same study showed a dyspareunia among 8.8% and chronic pelvic pain 5.5%.^[20] Our study showed 29.2% of dyspareunia and 42.2% had diffuse abdominal pain.

Incidence in Stages

In our previous study 21.1% had stage I endometriosis, 9.23% had stage II endometriosis whereas 35.4% had stage III endometriosis and 24.1% had stage IV endometriosis.

In our current study stage I and II endometriosis had only an incidence of 25%. Whereas Mishra *et al.*, 2017 study had 84% of stage I and II. The incidence of moderate and severe are found to be higher in our study 75% versus 15.93% in Mishra *et al.*, 2017 study the increasing incidence of severity of endometriosis in southern states could be explained by the regional variations.^[15] Combination of symptoms were also studied. 82.3% of the patients had minimum of 2 symptoms and 17.7% had 1 symptom. Asymptomatic endometriosis was seen around 13.5%. From this data we can infer if patients had more than two symptoms among 7 symptoms of endometriosis, we have to strongly suspect endometriosis.

Family History

The incidence of family history in our study was 13.5%. There is 6.9 times higher incidence of endometriosis among the family members.^[14] Family members were either mother, sisters or aunts.

There is a significant difference between the family history with regard to the symptoms experienced by the respondents. Further the mean scores reveal that the respondents with family history experience multiple symptoms than the other group [Table 2].

Menstrual history

Most of the patients had regular cycles 168/192 and the rest had irregular cycles, could be due to associated PCOS or anovulation.^[15]

Medical history

Diabetes and hypertension were seen in 3 patients each and 31/192 (16.14%) patients had hypothyroidism. In a study by Verma

et al., 2012 of 394 infertile women, 23.9% were hypothyroid (TSH >4.2 μ U/ml).^[39] No significant difference ($P = 0.058$) was observed in the mean (\pm SD) age between women with endometriosis (34.5 \pm 6.0 years) and controls (34.7 \pm 8.8 years). No significant difference was observed in the prevalence of thyroid disorders between women with endometriosis (38/661, 5.7%, 95% CI, 4.1–7.8) and controls (53/635, 8.3%, 95%CI, 6.3–10.8) ($P = 0.067$; 3.347 χ^2).

Women with mild (r-AFS stage I-II) and severe (r-AFS stage III-IV) endometriosis had similar prevalence of thyroid disorders ($P = 0.659$). The prevalence of thyroid disorders was also similar in infertile women with 11/155 (7.1%) and without endometriosis 8/115 (7.0%). Hypothyroidism was significantly less frequent in women with endometriosis (18/661, 2.7%, 95%CI, 1.6–4.3) than in controls (38/635, 6.0%, 95%CI, 4.3–8.1) ($P = 0.004$; 8.331, χ^2).^[40]

USG Findings

TV-USG can help us to diagnose endometriosis. Early diagnosis is made by probe tenderness which may be a surrogate marker for endometriosis. Endometrioma appears as an adnexal lesion with ground-glass homogenous opacities with kissing ovaries and it will indicate moderate to severe disease. As per IDEA group study DIE involving bladder and bowel can be picked up by various signs namely comet sign, Indian headdress or moose antler sign, pulling sleeve sign.^[10]

All our patients had TV-USG prior to laparoscopy. 25% of the patients did not have any imaging evidence of Endometriosis. Unilateral endometrioma was found in 40% and bilateral endometrioma was seen in 34.9%. Deep Infiltrative Endometriosis was seen in 23.95%, of which, 44% had associated unilateral endometrioma and 56% had bilateral endometrioma. Associated adenomyosis was seen in 18.75%. MRI was not performed in most of our patients. We relied upon USG.

Laparoscopic Findings

Gold standard in diagnosis of endometriosis is only through laparoscopy, endometriosis which is categorised into 4 groups based on r-ASRM score.^[41] Majority of the women who are infertile, do suffer from moderate to severe endometriosis. Presence of bilateral endometrioma or DIE has a strong correlation with a chronic pelvic pain. Minimal lesions may appear as small flakes or patches or polyps with red or brown color and as it becomes advanced there will be presence of black puckered or white fibrotic lesions. Apart from diagnosis, laparoscopy helps in treating the lesions. Minimal and mild lesions are treated by cauterization, laserization or local excision. Laufer *et al.*, 1997 and Brosens *et al.*, 2001 recommend the technique of hydro floatation to visualise the early lesions like micro vascularization and adhesions.^[42,43] Some authors do pelvic peritonectomy for superficial endometriosis. Unilateral endometrioma was found in 40% and bilateral endometrioma was found in 34.9% of our study patients. Endometriomas were dealt by cystectomy which will prevent recurrence. Larger endometriomas sometimes need only cystostomy, as cystectomy might reduce their AMH level. DIE lesions are seen along with 30% of the endometriomas which also need excision. In our study 25% had minimal to mild disease which corresponds to the absence of USG finding. Pre laparoscopic USG can very well be correlated with the laparoscopic finding of unilateral and bilateral endometrioma. 36% of the cases had DIE. Whereas we could identify by USG only in 24%. All the patients had

hysteroscopy and chromotubation during laparoscopy. Peri-tubal adhesions, hydrosalpinx were seen in 14.06%. Tubes are invariably patent in majority of the endometriosis. After laparoscopy patients were allowed for spontaneous conception of OI with IUI for a period of 3 to 6 months in all the groups. In patients with tubal factor or male factor, patients were shifted to IUI or ART.

Associated Findings

- PCOS-12 (6.25%)
- Fibroids-5 (2.6%)
- Tubal diseases (Peri-tubal adhesions, hydrosalpinx) -27(14%)
- Mullerian anomaly-6 (3.1%) (Septate-4, bicornuate-1 and didelphys uterus-1)
- Laparoscopic findings based on revised AFS - Scoring and staging of endometriosis.

Patients with hydrosalpinx underwent cornual clipping in order to promote fertility subsequently when they undergo ART.^[44] 18.75% patients had adenomyosis, 6.25% patients had associated PCOS. Most of the patients with PCOS had stage I and stage II endometriosis and 2.6% patients had associated fibroid uterus.

6/192 (3.1%) patients had Mullerian anomalies; of which, 4 had septate uterus, one had bicornuate uterus and another had didelphys uterus. Mullerian anomalies are associated with higher incidence of endometriosis up to 75% especially in obstructed Mullerian anomalies. Whereas non-obstructive Mullerian anomalies were found to have 30.8% associated endometriosis.

Women with septate uterus have 26% incidence of endometriosis. Uterine dysperistalsis is found to be the cause for endometriosis among these patients.^[45] Septostomy was combined, when the patient underwent laparoscopy. No intervention was done for patients with bicornuate uterus or didelphys uterus.

CONCLUSION

Endometriosis is an enigmatic disease for both clinicians and the patients. There are two main problems associated with endometriosis, they are pain and infertility. Endometriosis associated pelvic pain is variable in pattern and intensity and affects the quality of life. There may be prolonged delay in diagnosis. This study has brought out the following points: 36% of patients who underwent laparoscopy for infertility had endometriosis. Primary infertility is more common than secondary infertility. There were many abortions in women with secondary infertility. Highest prevalence 57/192 (30%) was observed among the age group of 26-35 years (70%). Incidence is higher in upper middle class and upper class. 75% of our patients had moderate to severe endometriosis. Our patients with endometriosis had either low or normal BMI. Dysmenorrhoea was the commonest symptom observed among the study group (70.8%).

Asymptomatic patients were seen in 13.5%. Family history was observed in 13.5%. 75% of the women had USG evidence of endometrioma, either unilateral/bilateral. 24% had DIE, 18.75% had adenomyosis and associated other gynecological conditions like PCOS, fibroid, tubal diseases and Mullerian anomalies. Patients with history of severe dysmenorrhoea have to be investigated for endometriosis, especially laparoscopy, which will help to prevent the delay in diagnosis and prevent the progress of the disease and improve the quality of life.

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