Correlation of Pelvic Endometriosis with Infertility and Chronic Pelvic Pain: A Case Control Study

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Original Research Article

Abstract: Endometriosis the presence of functional endometrium outside the uterine cavity, is a chronic benign, estrogen dependent inflammatory disease that causing 35-50 % of woman having chronic pelvic pain and infertility. Aim was to analyse the association of endometriosis with chronic pelvic pain and infertility. This prospective case control study was carried out to predict strong association of symptoms of chronic pelvic pain & infertility with endometriosis. This study was conducted in department of Obstetrics and Gynecology, KGMU, Lucknow for a period of 1 year. Total number of woman enrolled in this study were 100 initially ,but finally 37 case of endometriosis with strong clinical features like dysmenorrhea, heavy or irregular per vaginal bleeding, dyspareunia, pelvic pain, lower abdomen pain and ultrasonography finding of endometriosis were included as case, they underwent laparotomy/laparoscopy. Control group comprises of 25 women undergoing for laparoscopic tubal ligation. The most common symptoms found in woman with endometriosis are dysmenorrhea (59.45%), dyspareunia (54.05%), menorrhagia (54.05%) and primary infertility (45.94%). p=0.001, p<0.001, p<0.001, p<0.001 respectively. The results indicate that there was statically significant difference in dysmenorrhea, dyspareunia, menorrhagia and primary infertility status of cases and control.
Keywords: Endometriosis, pelvic pain, infertility, dyspareunia, dysmenorrhea.

INTRODUCTION

Endometriosis is a pelvic inflammatory condition defined as the presence of ectopic deposit of endometrial tissue outside of the uterine cavity. The disease manifests clinically through various forms of pelvic pain or subfertility. The presence of pelvic endometriosis is about 5-10% in the general population, but in woman with pelvic pain, infertility, or both, the prevalence is 35-50% [1].The mechanisms contributing to the establishment of endometriosis lesions still remains controversial, despite extensive research. In fact, similar to tumors and their metastases, there is no doubt that long-term survival and proliferation of these lesions are crucially dependent on the formation of new blood vessels, which guarantee oxygen and essential nutrient supply [2-7] .Several growth factors and cytokines have been recognized as antigenic factors, such as interleukin-8 (IL-8), vascular endothelial growth factor (VEGF), TNF alfa [8-11].

MATERIALS AND METHODS

A prospective case control study was conducted from March 2013 to March 2014 at department of obstetrics and gynecology, KGMU, Lucknow. The study included 100 patients admitted in the department of obstetrics and gynecology, KGMU, Luck now, India. Out of 100 women, 75 women of reproductive age group with clinical suspicion and USG findings were taken as cases and 25 women of reproductive age group, who were undergoing laparoscopic bilateral tubal ligation were taken as control. Out of 75 cases, 12 cases lost the follow up and 26 cases kept on conservative management and they responded well. Finally 37 cases of endometriosis underwent laparotomy/laparoscopy (gold standard to diagnose endometriosis) for proper diagnosis and treatment.

Inclusion criteria includes all women aged between 10-45 years and patients with symptoms of Menstrual abnormality, severe dysmenorrheal, Premenstrual pain, Chronic pelvic pain, Dyspareunia,

GI complaints and Infertility was included in the study. Exclusion criteria were as follows patients with Acute Fever, Pelvic Inflammatory Disease (PID), and Urinary Tract Infection (UTI), chronic systemic illness (Diabetes Mellitus, Tuberculosis, Jaundice, and Immuno-compromised). Endometriosis was diagnosed during the laparoscopic procedure. The disease was staged according to the revised American Fertility Society (rAFS) classification. Laparoscopy was performed in post menstrual phase of cycle.

OBSERVATIONS

Table-1: Group Distribution of Study Population

S.No.	Group	Description	Number	Percentage
1-	Control	Women of reproductive age group undergoing laparoscopic tubal ligation	25	40.32
2-	Cases	Women with strong clinical suspicion, USG findings who underwent laparoscopic /laparotomy findings of endometriosis	37	59.68

Tabl-2: Age distribution of study group

Age (years)	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	**%**	**Number**	**%**	χ^2 **value**	**'p' value**
<18	7	18.92	0	0.00	21.967 (df=4)	<0.001
18-25	11	29.73	0	0.00		
25-30	16	43.24	14	56.00		
31-35	2	5.41	10	40.00		
>35	1	2.70	1	4.00		
	24.65+6.46 (Range 14-44 years)		30.88+2.28 (Range 28-36 years)		t=4.622; p<0.001	

Above data indicates that in both the group majority of subjects belonged to age group 25-30 years (Controls – 56%; Cases – 43.24%). In control group age of the subjects ranged between 28-36 years, 44% subjects belonged to age group >31 years including only 1 (4%) subject having age more than 35 years. Age of subjects included as Cases ranged between 14-44 years, 7 (18.92%) subjects belonged to age group <18 years, 11(29.73%) belonged to age group 18-25 years, 16 (43.24%) belonged to age group 25-30. Only 2 (5.41%) and 1 (2.70%) subjected belonged to age group 31-35 years and >35 years respectively. The above data indicate that subjects included in the study as Controls were having significantly higher (p<0.001) age (30.88+2.28 years) as compared to Cases (24.65+6.46 years).

Table-3: Habitat distribution of study population

Habitat	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Rural	12	32.43	13	52.0	2.374 (df=1)	0.123
Urban	25	67.57	12	48.0		

Above data indicates that majority of subjects included as Controls (52.0%) belonged to rural areas and rest 48.0% belonged to urban areas. Contrary results for subjects included as Cases were observed which indicates that 67.37% subjects belonged to urban areas and rest 32.43% subjects belonged to rural areas. The above difference was statistically non-significant.

Table-4: Religion belongs to study population

Religion	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Hindu	30	81.08	17	68.00	1.392 (df=1)	0.238
Muslim	7	18.92	8	32.00		

Majority of subjects in both the groups belonged to Hindu religion, though higher proportion of subjects (81.08%) included as Cases as compared to Controls (68.0%) followed Hinduism but this difference was statistically non-significant (p=0.238).

Table-5: Literacy status of study population

Literacy status	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Illiterate	6	16.22	13	52.00	8.988 (df=1)	0.003
Literate	31	83.78	12	48.00		

A significantly higher (p=0.003) proportion of subjects included in the study as Cases (83.78%) were literate as compared to proportion of subjects included as Controls (48.0%).

Table-6: Distribution of study population according to Marital Status

Marital Status	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Unmarried	9	24.32	0	0.00	7.114 (df=1)	0.008
Married	28	75.68	25	100.00		

None of the subject in Control group was unmarried while 9 (24.32%) subjects in Cases group were unmarried. There was statistically significant difference in marital status of cases and controls (p=0.008).

Table-7: Socioeconomic status (SES) of study population

Socioeconomic status (SES)	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Low	7	18.92	9	36.00	2.273 (df=1)	0.132
Average	30	81.08	16	64.00		

Above data shows that majority of patients in both the groups belonged to average socio-economic status. Though higher proportion of subjects included as Cases (81.08%) as compared Controls (64.0%) belonged to Average Socio-economic status but this difference was statistically non-significant.

Table-8: Distribution of cases according to clinical features (n=37)

Clinical Presentation	No. of Cases	Percentage
Dysmenorrhea	22	59.45
Dyspareunia	20	48.6
Menorrhagia	20	8.10
Primary Infertility	17	45.94
Secondary Infertility	4	10.8
Urinary Complaints	10	27.02
Amenorrhea	5	32.4

Table 9: Complaint of Dysmenorrhea in study population

Complaint of Dysmenorrhea	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Present	22	59.45	6	24.00	11.246 (df=1)	0.001
Absent	15	40.54	19	76.00		

Above data indicate significantly higher (p 0.001) proportion of subjects included as cases (59.45%) as compared to that as control (24.0%) were suffering from dysmenorrhea.

Table-10: Complaint of Dyspareunia in study population

Complaint of Dyspareunia	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Present	20	54.05	0	0.00	28.680 (df=1)	<0.001
Absent	17	45.95	25	100.0		

Only 20 subjects included as cases responded regarding dyspareunia. Above data indicate that none of the subject included as controls (0%) was suffering from dyspareunia while majority of subjects (54.05%) included as cases were suffering from Dyspareunia.

Table-11: complaint of Menorrhagia in study population

Complaint of Menorrhagia	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Present	20	54.05	3	12.00	14.871 (df=1)	<0.001
Absent	17	45.95	22	88.00		

In cases only 54.05% of subjects from the cases complaint of menorrhagia and only 12% controls complaint regarding menorrhagia which was found to be significantly higher in case.

Table-12: Infertility in study population

Infertility	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Primary	17	45.94	0	0.00	46.000 (df=2)	<0.001
Secondary	4	10.81	0	0.00		

Out of 21 respondents from Cases group, 17 (45.94%) subjects were suffering from primary infertility and 4 (10.81%) were suffering from secondary infertility. In rest cases 9 were unmarried and 7 subjects from cases had no complaint of regarding infertility. All the subjects included as Controls (100%) did not report any symptom of infertility. The results indicate that there was statistically significant difference in fertility status of cases and controls of regarding infertility.

Table-13: Urinary Complaint in study population

Urinary Complaints	Cases (n=37)		Controls (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Present	10	27.03	0	0.00	8.056 (df=1)	0.005
Absent	27	72.97	25	100.0		

None of the subjects included in the study as Controls (0%) reported any urinary complaint while a significantly higher (p=0.005) proportion of subjects as Cases (27.03%) reported urinary complaints. Maximum patients had dysuria and heaviness in lower abdomen.

Table-14: Complaint of Amenorrhea in study population

Complaint of Amenorrhea	Cases (n=37)		Control (n=25)		Statistical analysis	
	Number	%	Number	%	χ^2 value	'p' value
Absent	32	86.49	25	100.0	3.675 (df=2)	0.159
Primary	3	8.11	0	0.00		
Secondary	2	5.41	0	0.00		

Majority of the subjects (86.49%) included as cases do not complaint about amenorrhea. 3 (8.11%) cases reported primary amenorrhea in which 2 cases were unmarried and one case was married and 5.41% cases reported secondary amenorrhea. None of the subjects from control group complained of amenorrhea i.e. in all the subjects amenorrhea was found to be absent. Laparoscopy was done in these five cases for diagnostic purpose for amenorrhea and accidentally it was found that they had ovarian endometrioma or nodularity in posterior wall of uterus and pouch of douglus. Status of amenorrhea did not show any statistically significant difference between cases and controls.

Table-15: Finding of Per Vaginal Abnormalities in cases (n=17)

Nodularity in POD, tenderness present	1
Tenderness in B/L fornix	6
Uterus A/V Nodular swelling on episiotomy	1
Uterus A/V, Tenderness present in fornix	6
Uterus R/V, Tenderness present in fornix	3
Total	17

Table-16: Per Rectum Examination in Unmarried Cases (n=9)

Per Rectum Examination	Number	%
B/L ovarian mass felt	1	11.11
Fullness in POD	1	11.11
Left TO mass felt	1	11.11
Nodules felt in POD	3	33.33
Right TO mass	2	22.22
NAD	1	11.11

Per rectal examination was not done in control group and only unmarried subjects in the cases group were subjected to per rectal examination. Out of these 9 subjects, nodules were felt in POD in 3 (33.33%) subjects and Right TO mass was found in 2 (22.22%) subjects. No abnormality was detected in 1 (11.11%) subject.

In this study 21.62% cases had Bilateral ovarian endometrioma and 18.92% cases had endometriosis of pouch of douglus.

Table-17: USG finding in cases Population

USG reports	Cases (n=37)	
	Number	%
No report/not done	0	0.00
B/L ovarian endometriosis	8	21.62
Endometriosis of episiotomy scar	1	2.70
Endometriosis of POD	7	18.92
Endometriosis of POD & Lf ovary	1	2.70
Endometriosis of Right adnexa	1	2.70
Endometriosis of Right ovary	2	5.41
Endometriosis of Right ovary & POD	1	2.70
Left ovarian cyst	1	2.70
Left ovarian chocolate cyst	6	16.22
Right ovarian endometriosis	7	18.92
Right TO mass	1	2.70
Scar endometriosis	1	2.70

Table-18: Patient's characteristic

Variable	Category	Controls	Cases	Total	OR (95% CI)	'p' value
Age (years)	Mean+SD (n)	30.88+2.28 (n=25)	24.65+6.46 (n=37)	27.16+6.01 (n=62)	(3.535-8.928)	<0.001
Education	Illiterate	13	6	19	OR=2.80 (1.00-7.834)	0.003
	Literate	12	31	43		
Married	Married	25	28	53	–	0.008
	Unmarried	0	9	9		
Amenorrhea	Yes	0	5	5	–	0.055
	No	25	32	57		
Dysmenorrhoea	Absent	19	3	22	OR=23.22 (5.101-05.728)	<0.001
	Present	6	22	28		
Dyspareunia	Absent	25	8	33	–	<0.001
	Present	0	18	18		
Infertility	Absent	0	16	16	–	<0.001
	Present	25	21	46		

DISCUSSION

In our study it was found that the group majority of subjects belong to age group 25-30 years. It indicates that subjects included in the study as Controls were having significantly higher (p<0.001) age (30.88+2.28 years) as compared to Cases (24.65+6.46 years). The mean age was 24.65 years (Table 2).The study conducted by W.P. Dmowski [12] included subjects predominantly of childbearing age. The mean age at diagnosis is 25-29 years and another study done by Wachyu Hadisaputra[13]. They included the subjects with mean age of endometriosis subjects was 32.8±4.7 years, and mean control age was 36.2±4.0 years (P: 0.001, 95% CI 1.4-5.3). In our culture, women usually marry between 20 and 30 years of age and seek medical assistance if no conception occurs within a year. Most

of them undergoes laparoscopic examination. Women with high level of education are usually established financially and have means to undergo medical treatment. Patient with endometriosis were younger and educated than control group. In our study majority of subjects belong to Hindu religion but this difference is non-significant. Makhlouf Obermeyer C *et al.* [14] concluded that there is no association between endometriosis and religion and nationality(Table4). Present study shows significantly higher (p=0.003) proportion of subjects included in the study as Cases (83.78%) were literate as compared to proportion of subjects included as Controls (48.0%).

Our study is conducted by Zhonghua Yi Xue Za Zhi. [15] showed that there is an increased risk for endometriosis in women who had a higher level of education so that literacy play important role in development of endometriosis (Table 5). In our study, 75.68% cases were married and 24.32% were unmarried. A study done by Wachyu Hadiaputra [13] showed, almost all women (96.2%) were married (Table 6). Signorello LB [16] concluded that endometriosis is frequently seen in high socioeconomic status. In present study which shows that higher proportion of subjects included as Cases (81.08%) as compared Controls (64.0%) belonged to Average Socio-economic status (Table 7). The most frequently symptoms found in women with endometriosis are dysmenorrhea (59.45%), dyspareunia (48.60%), menorrhagia (8.1%) and primary infertility (45.94%) (Table9). E.B. Janssen [17] in which he concluded that most common cause of secondary dysmenorrhea is endometriosis, which can be visually confirmed by laparoscopy in approximately 70% of adolescents with dysmenorrhea. Our study was supported by Ballard *et al.* and Ferrero *et al.* [18] according to that endometriosis is the most frequent cause of deep dyspareunia, and patients with the disease have a 9-fold increase in risk of experiencing this symptom when compared with the general female population (Table 10). In present study 56.7% subjects had infertility (both primary and secondary), it was advocated by Tomassetti C [19] who stated that endometriosis can lead to anatomical distortions and adhesions (the fibrous bands that form between tissues and organs following recovery from an injury). They are many theories suggesting the relationship between infertility and endometriosis. These include increased number of peritoneal macrophages that might phagocytise spermatozoa, increased concentration of peritoneal cytokines that might impair ovulation, and the presence of autoantibody antialanin-111, which plays a role in the implantation failure [6]. Other risk factors include dysmenorrhea and chronic pelvic pain. Chronic pelvic pain might be due to irritation or direct infiltration of the nerve on the pelvic floor by endometriosis. It usually occurs when the endometriosis lesion is located on the lateral pelvic wall and in the presence of adhesions (Table 12).

On pelvic examination, the objective signs of women with endometriosis vary according to the location and size of lesion. One may find TO mass in adnexa, nodules in pouch of douglus, cervical tenderness. We found that sensitivity was low but specificity was high. It seems that in our study all patients with palpable rectovaginal nodule had endometriosis. A study done by Matorras R [20] who concluded that endometriomas may be detected as tender or nontender adnexal masses, often fixed to the uterus or to the pelvic sidewall. Tender masses, nodules, and fibrosis may be appreciated on palpation of the upper vagina, cul-de-sac, uterosacral ligaments, or rectovaginal septum. In a case-controlled study, the only signs of endometriosis in infertile patients were uterosacral nodularity and uterosacral tenderness.A study done by Wachyu Hadisaputra showed that the prevalence of endometriosis lesion on the posterior fornix was 10 %, and on the rectovaginal septum was 25 %. Rectovaginal nodule develops due to chronic endometriosis causing fibrotic nodule containing endometrial tissue, mixed with fat and fibromuscular tissue (Table 15,16). In our study according to USG finding we found that 8 cases had B/L ovarian endometrioma, 7 cases had endometriosis of pouch of douglus., but the non-invasive approaches such as ultrasound, magnetic resonance imaging or blood tests have not yielded sufficient power for the diagnosis of endometriosis[21] (Table 17).

RESULTS

The following resultswas drawn from the observation and discussion made in the present study:-

- Above data indicates that in both the group majority of subjects belonged to age group 25-30 years (Controls – 56%; Cases – 43.24%).The mean age in control group (n=25) was 30.88+2.28 years and in study group mean age was 24.65+6.46 years. Majority of women were in age group 18-25 years (29.73%) (Table 2).

- There were no significant association of religion and habitat found with development of endometriosis.(Table 3and 4).

- There is significantly higher (p=0.003) proportion of subjects included in the study as cases (83.78%) were literate as compared to proportion of subjects included as Controls (48.0%) (Table 5).

- 28 cases (75.68%) were married and 9 cases (24.32%) were unmarried. none of the subjects in control were unmarried (Table 6).

- The majority of patients (81.8%) in both the groups belonged to average socio-economic status. The difference was statistically non-significant (Table 7).

- There was significantly higher (p<0.001) proportion of subjects included as cases (59.45%) as compared to that as control (24.0%) were suffering from dysmenorrhea (Table 9).

- The majority of subjects (54.05%) included as cases were suffering from dyspareunia suggesting

strong association of dyspareunia with endometriosis (Table 10).

- In this study 54.05% cases complaint of menorrhagia and only 12% control had menorrhagia which was found to be significantly higher in cases (Table 11).
- It was found that out of 37 cases of endometriosis, 21 respondents had infertility, 17 (45.94%) subjects were suffering from primary infertility and 4 (10.81%) were suffering from secondary infertility. The results indicate that there was statistically significant difference in fertility status of cases and controls (Table 12).
- There was significantly higher (p=0.005) proportion of subjects as Cases (27.03%) reported urinary complaint. Maximum patients had dysuria and heaviness in lower abdomen (Table 13).
- The majority of subjects had normal menstrual history. Only 5 cases had amenorrhea. The Status of amenorrhea did not show any statistically significant difference between cases and controls (Table14).
- Out of 37 cases, 45.95% cases had abnormal per vaginum examination, maximum cases had tenderness in fornix. (Table 15).
- Per rectal examination was done in unmarried cases (n=9), out of which 33.33% had nodules in pouch of douglus and 22.22% had TO mass (Table 16).
- Cases included in study, 21.62% cases had bilateral ovarian endometriosis in ultrasonography findings. 18.92% cases had endometriosis of pouch of douglus (Table17).

CONCLUSION

Endometriosis is significant cause for chronic pelvic pain, dyspareunia, menorrhagia and infertility, is a major discomfort for woman in all over the world from the view of medical management that of social cost.

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