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Original Article

Co-Existence of Uterine Myomas and Endometriosis in Women Undergoing Myomectomy/Hysterectomy

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ABSTRACT

Objective: To determine the frequency of coexistence of myomas and endometriosis in patients undergoing myomectomy or hysterectomy.

Study Design: Cross-sectional study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi, Pakistan from Sep 2022 to Sep 2023.

Methodology: Seventy (70) patients undergoing above mentioned myomectomy/hysterectomy were visually examined for the presence of endometriosis. The Chi-square test and Fisher's exact test were used in SPSS-20 to determine the significance of the relationship between the two conditions. Categorical data were expressed as descriptive statistics through frequency percentile. Analysis of continuous variables was carried out through the one-way ANOVA. Results were considered significant at $p \leq 0.05$.

Results: In this study, 13 out of 70(18.57%) of the patients operated for myomectomy/ hysterectomy were found to have coexisting uterine myomas and endometriosis. Statistically non-significant (p=0.08) association between these two ailments was noted. Age, parity and body weight were not found to influence the existence or coexistence of these ailments. Pain was a significant finding 13(18.57%) in cases of endometriosis and coexisting uterine myomas (p=0.00). Abnormal uterine bleeding was found significantly (p=0.02) associated with uterine myomas 54(77.14%). Subfertility though a predominant feature was not found to have a significant association with both the conditions and their coexistence (p=0.35, p=0.34 & p=0.44).

Conclusion: A non-significant association between uterine myomas and endometriosis. Pain was a significant finding where the two diseases coexisted.

Keywords: Comorbidity, Endometriosis, Hysterectomy, Myomas.

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INTRODUCTION

Uterine myoma and endometriosis are two major causes of gynaecological complaints, among women. Myomas by definition are benign tumours of the myometrium developing in smooth musculature. Structurally these are composed of glycoproteins and collagen fibers. Fibroids have a spectrum of symptoms in women ranging from mild pain or pressure, difficulty in urinating or defecating to heavy menstrual bleeding which sometimes can be life-threatening. In such conditions, surgical intervention like myomectomy or hysterectomy is advised. Endometriosis, on the other hand, involves the presence of endometrial glands and stroma at extra-uterine locations. Due to severe pain associated with this condition, surgical intervention is usually required. These two are though, benign conditions of the uterus, but may adversely affect the reproductive life of a woman.[1,2] Infertility and poor health are major outcomes of these issues; however, untreated cases may lead to serious complications. Each one of the two has its effects on patients' health; however, simultaneous presence may aggravate the condition. Patients suffering from either or both of these conditions have poor life quality due to variable complaints which include voluminous menstrual bleeding or menorrhagia, anaemia, painful periods, urinary incontinence, discomfort during sex, constipation, backache, lower abdominal as well as pelvic pain and poor fertility.[3] Uterine myomas are enormously common conditions in women over 45 years of age where an incidence of over 60% has been reported.[4] In an earlier study conducted at Rawalpindi, Pakistan, more than 50% of the women reporting at a tertiary care centre with menstrual irregularity were diagnosed to have uterine myomas out of which 77.14% were multiparous.[5] Sometimes myomas are incidental finding during surgeries planned for other malignant and premalignant diseases like severe adenomyosis and deeply infiltrating endometriosis. When myomas and endometriosis co-occur, clinicians face a complex decision-making process regarding the appropriate surgical approach, as well as considerations for fertility preservation.

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This study aimed to report the prevalence of co-existence of uterine fibroids and endometriosis noticed during surgical interventions and establish a correlation if any between the two conditions as well as enumerate the risk factors associated with them. If any association is established between myomas and endometriosis, new non-invasive treatments and pharmacotherapies can be developed to target these conditions.[6]

METHODOLOGY

This cross-sectional study was carried out at the Department of Obstetrics & Gynaecology, Pak Emirates Military Hospital, Rawalpindi Pakistan from September 2022 to September 2023 after seeking approval vide number CPSP/REU/OBG-2021-124-10954 dated 27 August 2022. Formal ethical approval was obtained from the hospital Ethical Review Committee (A/28/ERC/619/23). Sample size was calculated using WHO sample size calculator,[7] with the reported prevalence of uterine myometra 40%.[8] The estimated sample size came out to be 369; however, for this study only 70 women patients could be made available.

Inclusion Criteria: Patients aged between 20 to 60 years, both nulliparous and parous, who were pre-diagnosed with either fibroids or endometriosis clinically or on ultrasound/MRI or had severe symptoms indicating exploration via open surgery/laparoscopy were included.

Exclusion Criteria: Patients who had well established and diagnosed co-occurrence of both conditions were excluded from the study.

A total of seventy patients who underwent myomectomy or hysterectomy during the above mentioned study duration were included in the study. Pre-operatively, all patients were assessed and detailed history and examination were taken. Age, parity, marital status and primary complaints were taken as variables. Endometriosis was diagnosed during laparotomy/laparoscopy by visualisation of deposits of endometrial tissue on the outer surface of the uterus, fallopian tubes, ovaries, peritoneum or any other organs. In cases where no gross deposits were seen but patients had significant history, further confirmation was made through histopathology.

Data was entered in an excel sheet for subsequent analysis. Categorical data like the presence or absence of disease were expressed as descriptive statistics through frequency percentile. To determine the association between categorical variables, data collected were cross-tabulated and subjected to statistical analysis under the Chi-square test using SPSS version 20. The coefficient of association was calculated in a 2x2 cross table. Analysis of continuous variables was carried out through one-way analysis of variance (ANOVA) in SPSS. Results were considered significant at $p \leq 0.05$.

RESULTS

The mean age and body mass index (BMI) of the subjects were 37.57±5.60 years and 26.7±5.0 (kg/m²) respectively whereas parity ranged from 0 to 6. Overall abnormal uterine bleeding was the major complaint 54(77.14%) followed by subfertility 40 (57.17%) and pain 35(50%). During surgery 63(90%) patients were found to have myomas whereas endometriosis was the least common finding 13(18.57%). Thirteen (18.57%) of the patients operated for myomectomy/hysterectomy were found to have coexisting uterine myomas and endometriosis. The statistical analysis showed a non-significant association between the two ailments (p=0.08, Table-I). Age (p=0.97) and body weight (p=0.16) were not found to influence the existence or coexistence of these ailments (Table-II). Pain was a significant finding in endometriosis 13(18.57%, p<0.001) and when

Table-I Coexistence of Gynaecological Conditions Observed During Surgery (n=70)

Baseline Characteristics of Patients		Prevalence of Uterine Myomas n(%)		Total	*p*-value
		Present	Absent		
Prevalence of Endometriosis n(%)	Present	10(14.28%)	3(4.29%)	13(18.57%)	0.08
	Absent	53(75.71%)	4(5.71%)	57(81.42%)	
Total		63(90%)	7(10%)	70(100%)	

Table-II Association of Gynaecological Conditions with Patient Demographics (n=70)

Variables	Diseases			*p*-value
	Myomas	Endometriosis	Myomas+ Endometriosis	
Age (Years) (Mean±SD)	37.68±6.05	35.00±10	37.50±3.80	0.97
Body weight (Kilogram) (Mean±SD)	66.25±7.75	61.00±5.29	61.30±5.10	0.16

ANOVA

Table-III Association of Gynaecological Conditions with Pain (n=70)

Uterine Myometra					
Baseline Characteristics		**Abdominal/pelvic pain n(%)**		**Total**	***p*-value**
		Present	**Absent**		
Prevalence n(%)	Present	30(42.86%)	33(47.14%)	63(90.00%)	0.06
	Absent	6(8.57%)	1(1.43%)	7(10.00%)	
Total		36(51.43%)	34(48.57%)	70(100.00%)	
Endometriosis					
Baseline Characteristics		Abdominal/pelvic pain n(%)		Total	*p*-value
		Present	Absent		
Prevalence n(%)	Present	13(18.57%)	0(0.00%)	13(18.57%)	<0.001
	Absent	23(32.86%)	34(48.57%)	57(81.42%)	
Total		36(51.43%)	34(48.57%)	70(100.00%)	
Myometra coexisting with Endometriosis					
Baseline Characteristics		Abdominal/pelvic pain n(%)		Total	*p*-value
		Present	Absent		
Prevalence n (%)	Present	10(14.28%)	0(0.00%)	10 (14.28%)	<0.001
	Absent	26(37.14%)	34(48.57%)	60 (85.71%)	
Total		36(51.43%)	34(48.57%)	70(100.00%)	

Table-IV Association of Gynaecological Conditions with Abnormal Uterine Bleeding (n=70)

Uterine Myometra					
Baseline Characteristics		**Uterine Bleeding n (%)**		**Total**	***p*-value**
		Present	**Absent**		
Prevalence n(%)	Present	54(77.14%)	9(12.86%)	63(90.00%)	0.02
	Absent	4(5.71%)	3 (4.29%)	7(10.00%)	
Total		58(82.85%)	12(17.15%)	70(100.00%)	
Endometriosis					
Baseline Characteristics		Uterine Bleeding n(%)		Total	*p*-value
		Present	Absent		
Prevalence n(%)	Present	9(12.86%)	4(5.71%)	13(18.57%)	0.33
	Absent	45(64.29%)	12(17.15%)	57(81.42%)	
Total		54(77.14%)	16(22.86%)	70(100.00%)	
Myometra coexisting with Endometriosis					
Baseline Characteristics		Uterine Bleeding n (%)		Total	*p*-value
		Present	Absent		
Prevalence n(%)	Present	8(11.73%)	2(2.86%)	10 (14.29%)	0.59
	Absent	46(65.71%)	14(20.00%)	60 (85.71%)	
Total		54(77.14%)	16(48.57%)	70(100.00%)	

Table-V Association of Gynaecological Conditions with Abnormal Subfertility (n=70)

Uterine Myometra					
Baseline Characteristics		**Subfertility n (%)**		**Total**	***p*-value**
		Present	**Absent**		
Prevalence n(%)	Present	35(50.00%)	28(40.00%)	63(90.00%)	0.35
	Absent	5(7.14%)	2(2.86%)	7(10.00%)	
Total		40(57.14%)	30(42.86%)	70(100.00%)	
Endometriosis					
Baseline Characteristics		Subfertility n(%)		Total	*p*-value
		Present	Absent		
Prevalence n(%)	Present	7(10.00%)	6 (8.57%)	13(18.57%)	0.33
	Absent	33(47.14%)	24(34.29%)	57(81.43%)	
Total		40(57.14%)	30(42.86%)	70(100.00%)	
Myometra coexisting with Endometriosis					
Baseline Characteristics		**Subfertility n(%)**		**Total**	***p*-value**
		Present	**Absent**		
Prevalence n(%)	Present	5(7.14%)	5(7.14%)	10 (14.29%)	0.59
	Absent	35(50.00%)	25(35.71%)	60 (85.71%)	
Total		40(54.14%)	30(42.86%)	70(100.00%)	

coexisting with uterine myomas 10(14.28%, $p<0.001$). However, it showed a weak association with myomas 30(42.85%, $p=0.06$) (Table-III). Abnormal uterine bleeding was found significantly ($p=0.02$) associated

with uterine myomas 54(77.14%), Table-IV). However, subfertility though a predominant feature was not found to have a significant association with myomas 35(50%), p=0.35), endometriosis 7(10%) and co-existing myomas and endometriosis 5(7.14%), p=0.59) (Table-V).

DISCUSSION

In our study, 18.57% of the patients operated for myomectomy or hysterectomy were found to have coexisting uterine myomas and endometriosis. Statistical analysis of the data collected revealed a non-significant association (p<0.08) between these two ailments. These findings are partly in line with previous studies carried out on the subject which have reported a highly variable (12-86%) prevalence of coexistence.[9] Huang *et al.*,[10] stated a frequency of 86% coexistence of these two conditions among 131 patients operated on for myomectomy or hysterectomy. A retrospective review by Nezhat *et al.*,[11] described a concomitant prevalence of myoma and endometriosis in 87% of the patients who underwent laparoscopic-assisted myomectomy or hysterectomy. A comparatively lower presence of coexistence (28.6%) was reported by Naphatthalung *et al.*,[12] Another study by Uimari *et al.*,[13] reported coexistence of 19.6% and 25.75% in the fibroid group and endometriosis group respectively. However, the said study did not find any association between the two diseases to affect fertility in women which is in agreement with our study. A comprehensive review carried out by Umari *et al.*,[14] reported contrasting results of a number of studies regarding the coexisting incidence of the two disorders. An interesting study carried out to analyze insurance claims in Korea showed a negative correlation between the two diseases.[15] Conversely, a similar study carried out in Taiwan described a significant correlation which confirmed the increased risk of endometriosis in uterine myoma-affected women.[16] Such large variation in prevalence can be attributed to a number of factors like less number of included patients, restriction of age limits, strict exclusion criteria, associating the coexistence to a specific type of myomas, diagnostic techniques, reliance on documented record of patients or a particular region under study. Retrospective studies and specificities of complaints lead to a population bias.[14] The lower comorbidity of the two diseases seen in our study might be due to our constraint to do it on patients only admitted during the study duration. A significant outcome of pelvic or abdominal pain and trend of abnormal uterine bleeding observed in our study is also in line with previous research by Uimari *et al.*,[14] and Nezhat *et al.*,[17] Co-occurrence of uterine myomas and endometriosis is a well-recognized phenomenon in the medical literature. Eighty percent of women by the age of 50 years are affected with some type of uterine myomas and another 10-15% of them suffer from endometriosis during their reproductive age.[18,19] Emerging evidence suggests that these conditions can coexist in a considerable proportion of women. It is therefore essential to know the pathophysiology of both conditions to understand the underlying mechanism leading to their co-existence. Both conditions are estrogen-dependent, and their co-occurrence may involve shared molecular pathways. Although the exact cause of uterine myomas is still unclear, the predisposing factors responsible for their development may include genetic susceptibility, growth factors and estrogenic hormones.[16] Endometriosis also remains an enigmatical condition, and the pathomechanism of its formation has yet to be definitively determined. Epigenetic changes, congenital traits, environmental influences, as well as histaminic reactions and auto-immune factors are often cited among the potential causes.[19] A recent study by Gallagher *et al.*,[20] carried out a meta-analysis of the genetic contribution to uterine myomas and identified four loci which were also associated with the risk of endometriosis. The said study reported that all of these four loci possess a gene carrying a signalling factor for female sex hormones oestrogen/progesterone underlying the biological aetiology of the two diseases.[20] Another variant of genetic risk factor was also reported by Fung *et al.*,[21] Uterine myomas are monoclonal cells which grow on activation of progesterone receptors by the oestrogen resulting in increased mitotic activity of secretory cells and cytogenic abnormalities.[22] Moreover, various growth factors like vascular, insulin type and epidermal, synergistically contribute to the effect of oestrogen and progesterone.[23] As for endometriosis foci, primarily the exciting factor is retrograde menstruation. The menstrual blood enters the peritoneal cavity through the fallopian tubes and in this way, exfoliated cells of endometrial origin get implanted at the surface of various organs.[19] Immunological disorders also play their role in the development of endometriosis, as an increased number of macrophages with compromised ability of phagocytic action against foreign cells are detected in the peritoneal cavity of affected patients.[23] In addition

inflammatory response coupled with immune reaction results in enhanced production of cytokines and prostaglandins which further aggravates the condition.[24] It is assumed that uterine myomas may disrupt the uterine surface thus causing an increase in retrograde menstruation which is the major risk factor leading to the formation of endometriosis. The findings of our study showed a moderate association between uterine myometras and endometriosis in the observed number of cases which was our limitation. Further studies are suggested to check the strength of this association. The apparent association between the two suggests that patients diagnosed with myomas should be suspected for endometriosis or vice versa. Patients undergoing elective myomectomy/ hysterectomy should be advised to give consent for the removal of any endometriosis tissue on detection during surgery.

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CONCLUSION

A coexistence of uterine myomas and endometriosis in 18.57% of the women undergoing myomectomy or hysterectomy. Statistical analysis showed a non-significant association between the two diseases. Age, parity and body weight had no influence on the prevalence of the two diseases. Pain was a significant feature in patients with comorbidity of the two diseases.

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Authors' Contribution

Th following authors have made substantial contributions to the manuscript as under:

AF & TY: Data acquisition, critical review, approval of the final version to be published.

BZ & HS: Conception, study design, drafting the manuscript, approval of the final version to be published.

5,6: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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