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ORIGINAL RESEARCH

Histopathological correlation of hysterectomy specimens with clinical and other investigational findings

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ABSTRACT

Context: Hysterectomy is the surgical removal of the uterus and is the most common major gynaecological surgical procedure performed worldwide.

Aims: To study the incidence and distribution of various types of pathologies in the hysterectomy specimens in the population studied.

Methods and Material: A total of 500 cases were studied. The study material was obtained from patients' hospitals that underwent hysterectomy and also specimens sent from nearby private or government

Results: Among various significant pathologies, benign accounted for 95.7% of lesions while malignant for 4.3% of lesions. Among benign lesions, adenomyosis was commonest with 203 (136 isolated + 67 with leiomyoma) cases and it was most common in 41-50 years age group. Leiomyoma was next common with 183 (116 isolated + 67 with adenomyosis) cases and it was also most common in 41-50 years age group. 67 (13.4%) cases had both leiomyoma and adenomyosis. CIN1 or LSIL accounted for 15 cases, serous cystadenoma of ovary for 12 cases, endometrial polyp for 12 cases, mature cystic teratoma of ovary for 8 cases, endocervical polyp for 9 cases, cervical leiomyoma for 6 cases, mucinous cystadenoma for 3 cases, placenta accreta for 3 cases, simple endometrial hyperplasia without atypia for 2 cases, infected decidua for 2 cases, CIN2/CIN3 or HSIL for 2 cases, adult granulosa cell tumour for 2 cases, endometriosis of ovary for 2 cases, broad ligament leiomyoma for 2 cases, acute salpingitis for 1 case, endometriosis of fallopian tube for 1 case, complete hydatidiform mole for 1 case, invasive hydatidiform mole for 1 case and adenomatoid tumour of myometrium for 1 case. Among malignant lesions, carcinoma of cervix was commonest with 11 cases, followed by carcinoma of ovary with 7 cases and carcinoma of endometrium with 3 cases.

Conclusions: This study provides baseline data to follow the trend of the hysterectomy and put insight into the pattern of complaints and preoperative diagnoses leading to hysterectomy as well as corresponding histopathological findings in the studied population. Histopathological examination is thus mandatory for confirming diagnosis and thus ensuring

optimal management to the patient, so every hysterectomy specimen should be subjected for histopathological examination.

Key-words: hysterectomy, endometrium, ovarian tumor, leiomyoma

INTRODUCTION

Hysterectomy is the surgical removal of the uterus and is the most common major gynaecological surgical procedure performed worldwide. In USA, hysterectomy is second only to cesarean section as the most frequently performed major operation and approximately 600,000 hysterectomies are performed each year.[1] In United Kingdom, 20% of women undergo hysterectomy before the age of sixty and approximately 100,000 hysterectomies are performed each year.[2]

Women aged 30 to 54 years more frequently undergo hysterectomy as compared to other age groups and contribute 74% of all hysterectomies.[3] According to center of disease control and prevention, around five per thousand women undergo hysterectomy annually in USA and one in four women will have hysterectomy by the age of 60 years.[4] Although vaginal hysterectomy is safer and cheaper than abdominal hysterectomy, the later still accounts for 60-80% of all hysterectomies and at least 95% of these are total rather than subtotal.[5]

The uterus is stimulated continually by hormones, denuded monthly of its endometrial mucosa and transiently inhabited by fetuses. It is subjected to a variety of disorders, the most common of which results from endocrine imbalances. Hysterectomy is most often indicated when medical treatment or less invasive methods have failed.[6] A total hysterectomy applies to the removal of the uterus and cervix. When bilateral adnexae are removed it is called as hysterectomy with bilateral salpingo-oophorectomy. Radical hysterectomy is a more extensive procedure done for cancer of uterus or cervix.[7]

AIMS AND OBJECTIVES

- To study the incidence and distribution of various types of pathologies in the hysterectomy specimens in the population studied.
- To review the major indications of all types of hysterectomy.
- To correlate histopathological findings with clinical features, pre-operative clinical diagnosis, radiological findings and other investigational findings if any.

MATERIALS AND METHODS

The present study is a prospective study performed on the hysterectomy specimens received at the department of surgical pathology from November 2020 to December 2021 irrespective of the clinical indications and type of hysterectomy.

A total of 500 cases were studies. The study material was obtained from patients' hospital that underwent hysterectomy and also specimens sent from nearby private or government

INCLUSION CRITERIA

- All hysterectomy specimens sent for histopathological examination at the Department of Surgical Pathology.

EXCLUSION CRITERIA

- None

Clinical and other pre-operative investigation details of the patients were obtained in consultation with the surgeon, patient records or laboratory records and entry was made in the prefoma.

Information was obtained regarding age, parity, presenting complaints, preoperative diagnosis/indication of hysterectomy, radiological and other pre-operative investigation findings, surgical procedure performed and the type of specimen sent.

Following the receipt of a specimen in jar containing 10% formalin, it was subjected to a thorough gross examination and was bisected and then kept for fixation in 10% formalin for 24-48 hours in the ratio of 1:10. After adequate fixation of the specimen, additional cut section morphology was recorded and appropriate sections were taken. The sections were processed and paraffin blocks were prepared. Sections were cut at 4-5 micron thickness and stained with hematoxylin and eosin**.** Detailed micro-anatomic features were then studied and recorded.

In case of more than one diagnosis, both diagnoses were counted by including them separately in their assigned category. Apart from physiological changes in the endometrium (e.g. secretory, proliferative, basal, atrophic etc.), chronic cervicitis or metaplasia that was not severe, ovaries with non-neoplastic/functional cysts that did not form the indication of hysterectomy and paratubal/paraovarian cysts or hydrosalpinx/hematosalpinx that were asymptomatic and just a chance finding were not considered pathological. Thus specimens with only one or more of the above findings were considered "unremarkable" histologically. The correlation between the histological findings and clinical and other investigational findings were estimated.

Further, the obtained parameters were evaluated using descriptive statistical analysis. Statistical analyses were performed using the IBM SPSS (Statistical Package for the Social Sciences v15.0 and Microsoft Excel 2007 software.

RESULTS

The maximum numbers of patients were 215 (43.0%) in the 41-50 years age group while the next in order of frequency was 191 (38.2%) in the 31-40 years age group. Of the 500 specimens, total hysterectomy with bilateral salpingo-oophorectomy was the commonest with 221 cases (44.2%), followed by total hysterectomy without salpingo-oophorectomy with 208 cases (41.6%), total hysterectomy with unilateral salpingo-oophorectomy with 68 cases (26.8%) and subtotal hysterectomy without salpingo-oophorectomy with 3 cases (0.6%). All the subtotal hysterectomy cases were of obstetric hysterectomy. Of the 500 hysterectomies, a maximum of 351 (70.2%) were of abdominal hysterectomy, followed by 80 (16.0%) of laparoscopic hysterectomy and 69 (13.8%) of vaginal hysterectomy. Maximum numbers of hysterectomies were done in patients having 1-3 parity. Table 1 shows the frequency of presenting symptoms of the patient. In many cases, the patient presented with more than one symptom.

Table/Fig 1: Distribution according to presenting symptoms of the patient

Symptom	No. of cases	Percentage %
Abnormal uterine bleeding	368	73.6
Abdominal pain	115	23.0
Discharge per vaginum	85	17.0
Something coming out per vaginum	58	11.6
Urinary complaints	39	7.8
Backache	13	2.6
Lump in abdomen	11	2.2
Weight loss	3	0.6
Difficulty in walking	3	0.6
Pain during intercourse	2	0.4
Others	2	0.4

Table 2 shows the frequency of endometrial findings in 500 specimens.

Table/Fig 2: Distribution of histopathological findings in the endometrium

Finding	No. of cases	Percentage %
Proliferative endometrium	209	41.8%
Secretory endometrium	108	21.6%
Basal endometrium	61	12.2%
Autolysed / disintegrated / not seen	41	8.2%
Atrophic endometrium	34	6.8%
Disordered proliferative endometrium	20	4.0%
Endometrial polyp	12	2.4%
Exogenous hormone changes	11	2.2%
Pregnancy changes	6	1.2%
Endometrial carcinoma	3	0.6%
Simple endometrial hyperplasia (without atypia)	2	0.4%
Infected decidua	2	0.4%
Hydatidiform mole	1	0.2%

Table 3 shows the frequency of myometrial findings in 500 specimens.

Table/Fig 3: **Distribution of histopathological findings in the myometrium.**

Finding	No. of cases	Percentage %
Unremarkable	176	35.2
Adenomyosis	136	27.2
Leiomyoma	116	23.2
Leiomyoma + adenomyosis	67	13.4
Placenta Accreta	3	0.6
Invasive hydatidiform mole	1	0.2
Adenomatoid Tumour	1	0.2
Total	**500**	**100**

Table 4 shows the distribution of histopathological findings in the cervix out of 497 specimens of hysterectomy containing cervix (as 3 cases were of subtotal hysterectomy). In many cases, two or more findings were present in the same case.

Table/Fig 4: **Distribution of histopathological findings in the cervix**

Findings	No. of cases	Percentage %
Chronic cervicitis	344	69.1
Nabothian cyst/s	225	45.2
Chronic active cervicitis	111	22.3
Squamous metaplasia	66	13.3
Papillary endocervicitis	40	8.0
Koilocytic changes	27	5.4
CIN1 or LSIL	15	3.0
Carcinoma of cervix	11	2.2
Squamous hyperplasia	10	2.0
Endocervical polyp	9	1.8
Cervical leiomyoma	6	1.2
Tunnel clusters	5	1.0
Glandular hyperplasia	3	0.6
CIN2 or CIN3 or HSIL	2	0.4
Haemangioma	2	0.4

Table 5 shows histological findings in the right and left ovaries separately.

Table/Fig 5: Distribution of histological findings in the ovaries.

Findings	Out of 261 right ovaries received		Out of 251 left ovaries received	
	No.	%	No.	%
Cystic follicle	110	42.1	101	38.7
Unremarkable	79	30.3	86	33.0
Haemorrhagic corpus luteal cyst	46	17.6	50	19.2
Follicular cyst	15	5.7	12	4.6
Serous cystadenoma	9	3.4	4	1.5
Corpus luteal cyst	9	3.4	4	1.5
Serous cystadenocarcinoma	6	2.3	5	2.0
Mature cystic teratoma	5	1.9	3	1.1
Mucinous cystadenoma	2	0.8	2	0.8
Adult granulosa cell tumour	1	0.4	1	0.4
Endometriosis	1	0.4	1	0.4

261 right ovaries and 251 left ovaries were received in 289 specimens of hysterectomy with either unilateral/bilateral salpingo-oophorectomy. In many cases, two or more lesions were present in the same ovary. Thus, out of 289 cases, there were 12 (4.2%) patients of serous cystadenoma, 8 (2.8%) patients of teratoma, 7 (2.4%) patients of serous cystadenocarcinoma, 3 (1.0%) patients of mucinous cystadenoma, 2 (0.7%) patients of granulosa cell tumour and 2 (0.7%) patients of endometriosis of ovary. In 44 (15.2%) patients, their ovary/ovaries were unremarkable. Table 6 shows histological findings in the right and left adnexae (fallopian tube, broad ligament, etc.) excluding ovaries.

Table/Fig 6: Histological findings in the adnexae (excluding ovaries)

	Right side	**%** (out of 261 right adnexae received)	**Left side**	**%** (out of 251 left adnexae received)
Unremarkable	235	90.0	210	83.7
Paratubal/parovarian cysts	13	5.0	16	6.4
Hydrosalpinx	12	4.6	19	7.6
Hematosalpinx	3	1.1	2	0.8
Broad ligament leiomyoma	2	0.8	0	0.0
Decidual reaction FT	1	0.4	2	0.8
Acute Salpingitis	0	0.0	1	0.4
Endometriosis FT	0	0.0	1	0.4

261 right sided and 251 left sided adnexae were received in 289 specimens of hysterectomy with either unilateral/bilateral salpingo-oophorectomy. In many cases, two or more lesions were present in the same adnexa. Table 7 shows various common histopathological lesions in 500 specimens. Pre-operative cervical biopsy was done in 34 patients.

Table/Fig 7: Common histopathological lesions along with patient's age correlation:

Age group	Adeno	Leio	Adeno + leio	CIN 1	SCA	EP	Ca cervix	CP	MCT	Ca. Ovary	CL	Ca. Endo
≤ 20	0	0	0	0	0	0	0	0	0	0	0	0
21-30	3	4	0	0	1	0	0	0	1	0	0	0
31-40	55	41	23	4	1	3	7	3	1	1	1	0

41-50	67	57	38	8	6	7	3	3	4	2	5	0
51-60	07	10	6	1	2	1	1	3	2	3	0	2
61-70	2	2	0	1	1	1	0	0	0	0	0	0
71-80	1	2	0	1	1	0	0	0	0	1	0	1
81-90	1	0	0	0	0	0	0	0	0	0	0	0
Total	**136**	**116**	**67**	**15**	**12**	**12**	**11**	**9**	**8**	**7**	**6**	**3**

Among 21 cases with finding of cervicitis/non-neoplastic lesions on cervical biopsy, histopathological findings of cervix in hysterectomy were consistent in 18 cases, while CIN1 was present in 2 cases and carcinoma of cervix in 1 case. Among 7 cases with CIN1 / LSIL on cervical biopsy, histopathological findings of cervix in hysterectomy were consistent in 4 cases while 3 cases showed only cervicitis. Among 2 cases with CIN2 / CIN3 / HSIL on cervical biopsy, histopathological findings of cervix in hysterectomy was consistent in 1 case while 1 case showed carcinoma of cervix. Among 4 cases with carcinoma of cervix on cervical biopsy, histopathological findings of cervix in hysterectomy were consistent with all the cases. Pre-operative endometrial biopsy was done in 46 patients. Among 40 cases with non-neoplastic findings in endometrial biopsy, histopathological findings of endometrium in hysterectomy were consistent with all of them. Among 3 cases with endometrial carcinoma on endometrial biopsy, histopathological findings of endometrium in hysterectomy were consistent with all of them. One case was diagnosed with hydatidiform mole on endometrial biopsy and was found to be invasive mole on USG. Hysterectomy was done which showed invasive hydatidiform mole on histopathology. One case was of incomplete abortion on endometrial biopsy; due to sepsis and continuous bleeding, hysterectomy was done, though no products of conception were seen during histopathology of the hysterectomy specimen. Pre-operative cervico-vaginal cytology (Pap smear) was done in 44 patients. All the 38 cases with finding of NILM with/without inflammation on Pap smear were in agreement with histopathological findings of cervix in hysterectomy specimens. Two cases with finding of ASCUS on Pap smear, histopathological findings of cervix in hysterectomy specimen showed non-neoplastic lesion in one case and CIN1 in other case. Among three cases with finding of SIL on Pap smear, histopathological findings of cervix in hysterectomy specimen showed non-neoplastic lesions in 2 cases and CIN1 in 1 case. One case with diagnosis of squamous cell carcinoma on Pap smear, histopathological finding of cervix in hysterectomy specimen also showed squamous cell carcinoma of cervix. In seven patients with ovarian cysts/tumours, preoperative serum CA-125 level was done. According to National Academy of Clinical Biochemistry (NACB), the cut-off value of serum CA-125 level for considering "normal" is 35 U/mL. In three of the benign ovarian neoplasms, CA-125 level was normal, in two of the benign ovarian neoplasms, CA-125 level was mildly increased and in two of the malignant ovarian neoplasms, CA-125 was abnormally high.

DISCUSSION

The peak age incidence of patients with hysterectomy was 41-50 years in studies performed by Shergill et al[8], Talukder et al[9], Gupta et al[10]**Error! Bookmark not defined.**, Perveen et al[11] and Samaila et al[12]. In the present study also, the peak age incidence of the patients was 41-50 years with 215 (43.0%) cases. In the present study, the patient's age range was 22-85 years and the mean age was 42.8 years, which are comparable to other studies. Abnormal uterine bleeding was the most common presenting symptom in 62.2% of cases in Khaniki et al[13] study, in 67.0% of cases in Qamar et al[14] study and in 66.0% of cases in Shergill et al[8] study. In the present study also, abnormal uterine bleeding was the most common presenting symptom in 73.6% cases. In a study by Perveen et al[11], benign lesions were more common (93%) as compared to malignant lesions (7%). This was also the case with Gupta et al[10]

where 96% of lesions were benign and 4% were malignant. In Pity et al[15] study, benign lesions were 93.9% and malignant lesions were 6.1%. In USA, 91.7% of hysterectomies are performed for benign conditions[i]. In the present study, benign lesions accounted for 95.7% while malignant lesions accounted for 4.3% of lesions, which is comparable to the other studies. Adenomyosis was the most common histopathological lesion in Sharqill et al[8] study (26.0% of cases). In the present study also, adenomyosis was the most frequent pathology in 27.2% of cases followed by leiomyoma in 23.2% of cases and combined leiomyoma with adenomyosis in 13.4 % of cases.

In studies by Jha et al[16], Riffat et al[17], Sobande et al[18] and Khaniki et al[13], leiomyoma was the most common pathology identified followed by adenomyosis. This variation with the present study could be due to differences, in varied population, of prevalence of risk factors in terms of quantities and type. Early menarche, delayed menopause, decreased parity, obesity and lack of exercise are some of the risk factors for leiomyoma. Also, diet has a role.[19,20]

In a study by Jamal et al[21], chronic cervicitis in cervix (41.53%) and functional cysts in ovaries (66.12%) were the most common histological findings. In our study also, chronic cervicitis in cervix (96.3%) and functional cysts in ovaries (32.6%) were the most common histopathological findings.

In a study by Sobande et al[18], leiomyoma was most common in 41-50 years age group (48%) and also adenomyosis, endometrial carcinoma and ovarian carcinoma were most common in 5th decade. In Perveen et al[11] study, leiomyoma was most common in 41-50 years age group (53.1%). Aboyeji et al [22]found that 78% of fibroid uterus occurred between ages 30-44 years. In the present study also, leiomyoma and adenomyosis were most common in 41-50 years age group.

In a study by Pity et al[15], no significant pathology was found in 24.8% of cases. Also, 'no pathology' was found in 21.4% of cases in Qamar et al[23] study, in 21.0% of cases in Khan et al[24] study, in 22.0% of cases in Lee NC et al[25] study, in 11.8% in Khaniki et al[13] study. In the present study, no significant pathology was found in 26.4% of cases, which is comparable to the other studies.

For cervico-vaginal cytology smears and histopathological findings correlation, the absolute concordance rate was 89% in a study by Joste et al[26], 91% in a study by Izadi-Mood et al[27], 88.5 % in a study by Tzeng et al[28] while it was 88.1% in a study by Adad et al[29]. In 44 cases of cervico-vaginal cytology in the present study, the findings were in agreement with histopathological findings in 93.2 % of cases, which is comparable with the others studies.

In a study by Bast et al[30], a raised level of antigen was detectable in the serum of 82% of women with epithelial ovarian cancer but in only 1% of healthy blood donors. CA-125 levels were raised above 35 U/ml in 78% of women with malignant masses, but also in 22% of those with benign masses in a study by Vasilev. [31]

In seven cases of ovarian cysts/tumours in the present study, preoperative CA-125 level was done. In three of the benign ovarian neoplasms, CA-125 level was normal, in two of the benign ovarian neoplasms, CA-125 level was mildly increased and in two of the malignant ovarian neoplasms, CA-125 was abnormally high. Thus it was in agreement with previous studies in predicting the chances of malignancy.

The use of serum CA125 levels in preoperative evaluation of tumor masses may not be used as the only means in malignancy prediction. CA125 in combination with other tests can be used in the differential diagnosis of pelvic masses and as part of the investigations for cancer screening. CA125 is an important indicator of response to treatment, guiding therapeutic decisions and identifying those patients whose response to chemotherapy and survival is short.[32]

CONCLUSION

This study provides baseline data to follow the trend of the hysterectomy and put insight into the pattern of complaints and preoperative diagnoses leading to hysterectomy as well as corresponding histopathological findings in the studied population. The most common pathologies identified on histopathological examination were adenomyosis, leiomyoma and cervical intraepithelial neoplasm 1 (CIN1). The most common clinical diagnoses/indications for hysterectomy were dysfunctional uterine bleeding, fibroid uterus and uterine prolapse. The final histopathological findings of the hysterectomy specimens correlates well with the preoperative clinical diagnosis, ultrasonography, cervical biopsy, endometrial biopsy, cervico-vaginal smear and tumour marker level findings. Histopathological examination is thus mandatory for confirming diagnosis and thus ensuring optimal management to the patient, so every hysterectomy specimen should be subjected for histopathological examination.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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