CLINICO-PATHOLOGICAL CORRELATION OF MORPHOLOGICAL LESIONS IN HYSTERECTOMY SPECIMENS - A 3-YEAR STUDY IN A MEDICAL COLLEGE HOSPITAL

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ABSTRACT

BACKGROUND

Hysterectomy is the most common procedure done for definitive treatment of abnormal uterine bleeding. However, advent of effective medical and conservative treatment modalities is now posing a question mark on justification of hysterectomy, thus advocating compulsory histopathological assessment to rationalise the need for hysterectomy procedures.

AIM

This study was done for identification of lesions of uterus and adnexa in routine hysterectomy specimens performed for various gynaecologic indications and correlation with the preoperative indications.

METHODOLOGY

A retrospective audit was done including hysterectomy specimens referred for gynaecologic indications to the Department of Pathology of a teaching hospital over a period of three years (May 2012- April 2015). All specimens were evaluated for clinical details and the frequency of various gross and microscopic endometrial, myometrial, cervical and adnexal changes.

RESULTS

During the study period, 826 hysterectomy specimens were received with most being simple hysterectomy specimens and the most common presenting symptom being menstrual irregularities (55.3%). Most of the women were in the age group of 31-50 years (75.5%). The most common preoperative indication in women less than 50 years of age was uterine fibroid and in women more than 50 years of age was prolapse. In the endometrium, most cases displayed proliferative phase (54.1%) and the most common pathological changes were endometrial polyp (9 cases) and simple hyperplasia (8 cases) followed by 2 cases of endometrial carcinoma, single case each of EIN and metastatic squamous cell carcinoma of cervix. In the myometrium, most common lesion was leiomyoma (40.4%). In the cervix, chronic cervicitis was most commonly observed. Fallopian tube was unremarkable in most cases (91.3%) and most ovarian specimens showed physiological changes (87.1%). The most common incidental finding was adenomyosis (20.7%).

CONCLUSION

Correlation of preoperative diagnosis to histopathological evaluation is essential for confirmation as well as identification of incidental findings that play a key role in morbidity of the patient. Adenomyosis still remains a clinical challenge elusive to preoperative diagnosis and thus, needs to be kept in mind by both clinician and pathologist for better patient management.

KEYWORDS

Hysterectomy, Abnormal Uterine Bleeding, Leiomyoma, Adenomyosis.

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INTRODUCTION: The uterus, composed of endometrium and myometrium, is amenable to continual alterations throughout a woman's life. These changes, range from the physiological alterations of menstrual cycle, pregnancy-related changes to pathological changes of hyperplasia and benign & malignant neoplastic lesions. Hysterectomy is the second most common major surgical procedure (following caesarean section) performed on women all over the world.[1]

In India, there are no national statistics available. However, there have been studies conducted in Haryana.[2] and Ahmedabad.[3] to assess the incidence and indications of hysterectomies in India. Hysterectomy specimens form the major proportion of specimens in the histopathological section of any hospital. It is the removal of uterus, either with (simple hysterectomy) or without cervix (supracervical hysterectomy) and unilateral (U/L) or bilateral (B/L) adnexa (total hysterectomy with U/L or B/L salpingo-oophorectomy respectively).[1] The most common indication for hysterectomy is abnormal uterine bleeding (AUB) due to any cause, which is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency or duration and occurs in the absence of pregnancy.[4]

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AUB occurs in women from 3rd to 6th decade due to various causes like uterine fibroids, chronic endometritis, endometrial polyps, adenomyosis and anovulation.[5] of which the most common are fibroids and adenomyosis.[4]

In the period of Hippocrates in 460-375 B.C., fibroids were known as the "uterine stone". Galen called this finding as "scleromas" during the second century of the Christian period. The term fibroid was coined by Rokitansky in 1860 and introduced in the 1863 by Klob. In 1854, Virchow demonstrated that fibroids were composed of smooth muscle cells and introduced the term "myoma".[6] The causes of fibroids are unknown and factors thought to be involved in their development and growth are hormonal factors like oestrogen & progesterone as well as insulin-like growth factors, epidermal growth factor and transforming growth factor.[7] Adenomyosis, which is also known as endometriosis interna, represents a diverticulosis of endometrium penetrating deeply into the myometrium.

The criteria adopted for diagnosis of adenomyosis include the presence of endometrial glands and stroma at a distance of more than one low power field in the myometrium when measured from the lower border of the endometrium.[8] Although there are minimal invasive surgical options like endometrial ablation, thermal balloon therapy and uterine artery embolisation available for the treatment of AUB, but due to the limited availability and cost, hysterectomy is still the most widely used definitive treatment procedure.[9]

AIMS & OBJECTIVES:

1. To study the various indications and patterns of lesions involving uterus and adnexa in hysterectomy specimens.
2. To study their correlation with the age and presenting symptoms of the patient.

METHODOLOGY: This was a retrospective audit carried out at the Department of Pathology of a medical college teaching hospital from May 2012 to April 2015. All the hysterectomy specimens following surgeries performed for gynaecologic causes were included in the study. Hysterectomy performed for obstetric reasons and uterus removal as part of post-mortem medico-legal evaluation were excluded. A total of 826 hysterectomy specimens were received during the study period. The specimens were labelled, formalin-fixed and subjected to routine processing and paraffin embedded, following which 5-6 microns thick sections were stained by haematoxylin & eosin stain. The specimens were evaluated for gross and microscopic features of uterine corpus, cervix and adnexa. Clinical details concerning the age, presenting complaints and indication for hysterectomy were obtained from the department records and histopathological requisition forms. Descriptive statistics were obtained using Microsoft Excel sheet.

RESULTS: During the study period, 826 hysterectomy specimens were received for histopathological evaluation, of which most women were in the age group of 41-50 years (329/826; 39.8%) followed by 31-40 years (295/826; 35.7%) - (Table 1). In our study, most women (396/826; 47.9%) presented with AUB followed by uterovaginal prolapse (290/826; 35.1%). Of the 826 cases in our study, 77 women presented with foul smelling discharge, lower abdominal pain and fever.

The most common preoperative indication for hysterectomy in women less than 50 years of age was fibroids (283/577; 49%), whereas in women more than 50 years it was uterovaginal prolapse (157/249; 63.1%). Among the 826 hysterectomy specimens, most (413/826; 50%) were simple hysterectomy specimens consisting of removal of uterus with cervix only, followed by total hysterectomy with B/L salpingo-oophorectomy (TAH & BSO) (289/826; 35%) and total hysterectomy with U/L salpingo-oophorectomy (124/826; 15%) - (Table 1). The most common preoperative indication was uterine fibroid (40.4%) in our study.

In 38 cases, preoperative diagnosis of dysfunctional uterine bleeding was made, wherein no structural abnormalities were observed on clinical and radiological examination. Of these, 17 cases were confirmed on histopathology with the absence of any pathology and in 08 cases adenomyosis was seen.

Age Distribution (In Years)	**Type of Hysterectomy (n=826)**			**Total**
	Simple Hysterectomy	TAH with U/L SO[#]	TAH with B/L SO[#]	
< equal to 30	010	011	006	027
31-40	126	070	099	295
41-50	140	038	151	329
51-60	085	002	023	110
61-70	045	002	008	055
> 70	007	001	002	010
Total	**413**	**124**	**289**	**826**

Table 1: Age Distribution in Correlation with the Type of Surgery Performed

[#]SO- salpingo-oophorectomy

Changes in Endometrium: Out of 826 specimens, simple hyperplasia was observed in 18 cases (2.2%) - (Figure 1), complex hyperplasia without atypia in 7 cases (0.8%) and endometrial adenomatous polyp in 19 cases (2.3%). Endometrial intraepithelial neoplasia was seen in one case, invasive endometrial carcinoma in 02 cases and metastatic squamous cell carcinoma from cervix was observed in 01 case. Proliferative endometrium was seen in 447 cases (54.1%), secretory endometrium in 136 cases (16.5%) and atrophic endometrium in 192 cases (23.2%).

Changes in myometrium: Of the 826 cases, 334 cases showed leiomyoma, of which 278 were intramural, 02 were submucous and 16 were subserosal in location. Multiple fibroids were seen in 38 cases. Coexisting leiomyoma and adenomyosis was observed in 63 cases (Table 2) - (Figure 2 & 3). Endometrial findings were correlated with the 334 cases of symptomatic fibroids, of which 230 cases showed proliferative phase, 63 cases showed secretory phase, 22

cases showed atrophic change, 7 cases showed endometrial polyp, 08 cases showed simple hyperplasia, 03 cases complex hyperplasia without atypia and 01 case showed complex hyperplasia with atypia. Of the 290 cases of prolapse, most common endometrial change was atrophy of endometrium (154/290; 53.1%). (Table 3).

Histological Lesions	Number of Cases
Leiomyoma	271
Adenomyosis	171
Dual pathology	063

Table 2: Distribution of Myometrial Lesions

Changes in endometrium	Location of leiomyoma (n=334)			
	Submucous	Subserosal	Intramural	Multiple
Proliferative phase	02	09	195	24
Secretory phase	00	04	51	08
Simple hyperplasia	00	02	05	01
Complex hyperplasia without atypia	00	00	02	01
Complex hyperplasia with atypia	00	00	01	00
Endometrial polyp	00	01	05	01
Atrophic endometrium	00	00	19	03
Total	02	16	278	38

Table 3: Endometrial Changes Associated with Fibroid

Adenexa were removed in 416 cases and displayed predominantly physiological changes. (Table 4)

Histopathology of the Ovary	Total
Physiologic (n=362)	
Follicular cyst/CH/CL	362
Non-neoplastic lesions (n=3)	
Ovarian torsion	001
Oophoritis	001
Endometriosis	001
Neoplastic (n=51)	
Serous cyst adenoma	024
Mucinous cyst adenoma	010
Serous cyst adenoma (borderline)	001
Mucinous cyst adenoma (borderline)	002
Serous cyst adenocarcinoma	002
Mucinous cyst adenocarcinoma	001
Mature cystic teratoma	007
Teratoma with Squamous cell carcinoma	001
Granulosa cell tumor (Figure 4)	001
Sertoli cell tumor (Figure 5)	001
Benign Brenner tumor	001

Table 4: Histopathological Findings in the Ovaries (n=416)

In our study, we observed a multitude of incidental findings, which were not diagnosed preoperatively, ranging from benign lesions like adenomyosis to premalignant lesions like CIN and CIS and invasive carcinoma. The most common incidental finding in our study was adenomyosis (20.7%).

We also observed premalignant changes in 10 cases in cervical epithelium, endometrial carcinoma in one case and one case showing endometrial hyperplasia. (Table 5)

Incidental Findings/Secondary Changes	Cases (%)
Adenomyosis	171 (20.7)
Senile cystic change	150 (18.2)
Endometrial polyp	019 (2.30)
Endometrial hyperplasia/carcinoma	002 (0.20)
Endometriosis	001 (0.10)
Cervical premalignant changes	010 (01.0)
Chronic endometritis	001 (0.10)
Hydrosalpinx/salpingitis/endometriosis	030 (03.0)

Table 5: Incidental Histopathological Findings and Secondary Changes

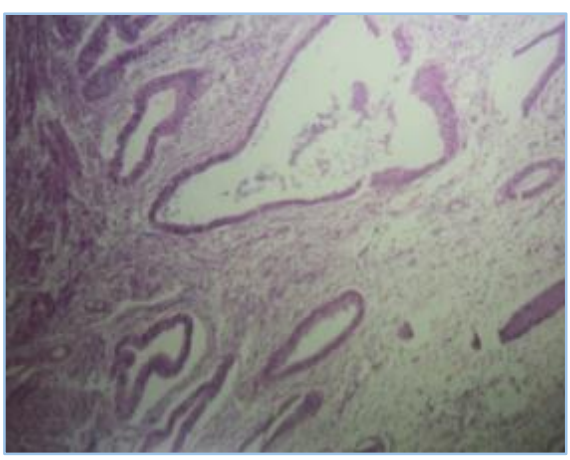

Fig. 1: Microphotograph Showing Cystically Dilated Endometrial Glands Displaying Hyperplasia (H & E, x 10)

Fig 2: Gross Photograph (A), Small Fibroid with Trabeculated Appearance of Adenomyosis (arrow), (B) Fibroid showing Myxoid & Cystic Degeneration (C), Multiple Fibroids

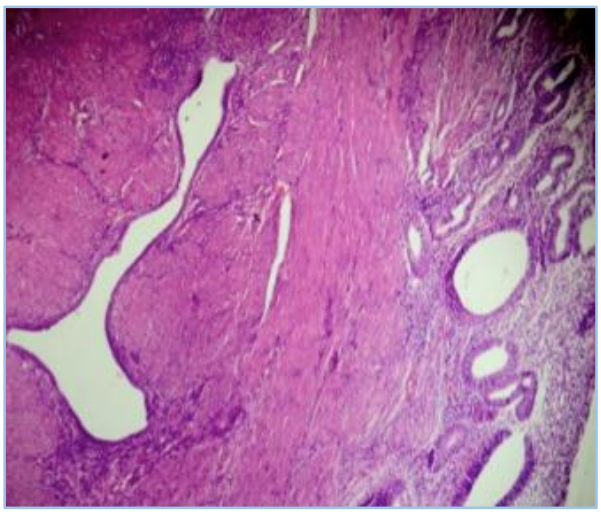

Fig. 3: Microphotograph showing Adenomyosis (H & E, x 10)

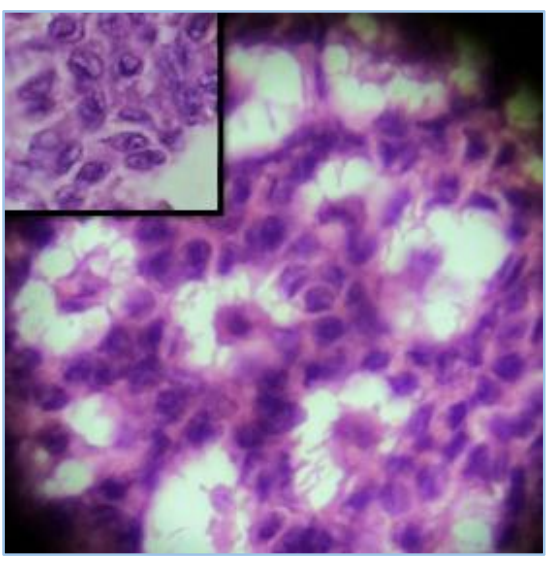

Fig. 4: Microphotograph Showing Call-Exner bodies in Granulosa cell Tumor (H & E, x 40); Inset: Nuclear Grooves (H & E, x 100)

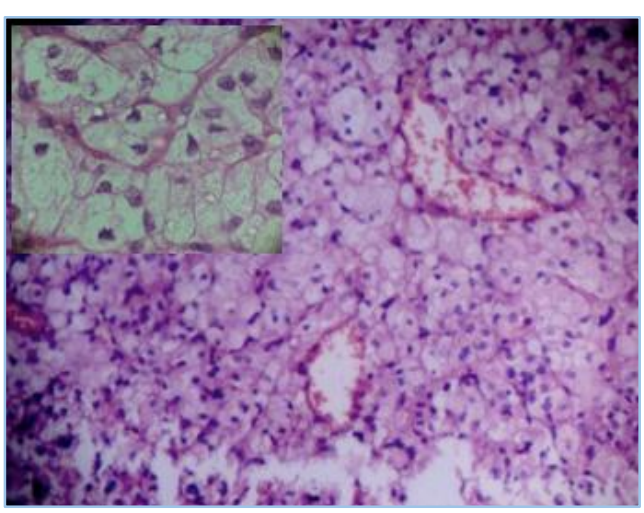

Fig. 5: Microphotograph Showing Occasional tubules of Sertoli-like cells (H & E, x 10); Inset: Tumor Cells Having Pale Eosinophilic clear to Vacuolated Cytoplasm with oval Elongated (H & E, x 100) nuclei Displaying Occasional Nucleoli (H & E, x 10)

DISCUSSION: Charles Clay performed the first subtotal hysterectomy in Manchester, England, in 1843 and first total abdominal hysterectomy in 1929. Since early 20th century, hysterectomy is a definitive treatment of pelvic pathology including fibroid, abnormal uterine bleeding, chronic pelvic pain, endometriosis, adenomyosis, uterine prolapse, pelvic inflammatory disease and genital malignancies.[10] In the present study, most (39.8%) women were in the age group of 41-50 years of age, similar to studies done by Vaidya S et al[11] (45.63%) and Rather et al[12] (47.27%). The mean age in our study was 45.54 years, similar to the studies done by Rahat Sarfaraz et al[13] (44.58 years) and Vaidya S et al[11] (46.98%).

Abnormal uterine bleeding (AUB) occurs in 9-14% of women between menarche and menopause, significantly impacting quality of life and imposing financial burden. The aetiologies of AUB are classified as related and unrelated to structural uterine abnormalities and categorised following the acronym PALM-COEIN: polyp, adenomyosis, leiomyoma, malignancy & hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not otherwise specified.[4] In our study, abnormal uterine bleeding was the most common clinical presentation (47.9%), similar to Rather.[12] et al and Saleh et al.[11] Hysterectomy can be done by abdominal, vaginal and laparoscopic approaches of which abdominal approach is the most preferred all over the world. All the hysterectomies were done by abdominal approach in our study. Similarly, a higher percentage has been reported in other studies.[1,4,9,10,11,12] The most common type of hysterectomy was simple hysterectomy (50%), followed by TAH with BSO in our study. However, in studies done by Rather et al[12] and Vaidya et al[11], TAH with BSO was the most common type of operative procedure.

The most common preoperative indication in our study was fibroids (40.4%), similar to studies done by Deeksha Pandey.[1] et al (39.8%), Vaidya et al[11] (42.94%) and dissimilar to study done by Rather et al[12] in which the most common indication was menorrhagia followed by fibroids. However, while correlating age with the preoperative indication, in women less than 50 years, the most common indication was fibroids (49%) and in more than 50 years of age, it was uterovaginal prolapse (63.1%). Leiomyoma occurs chiefly in women during active mid-reproductive years, presenting most commonly with AUB (65.2%), which is due to the increased size of uterine cavity thereby increasing the surface area of the endometrium, hyperoestrogenaemia causing endometrial hyperplasia, vascular alterations of the endometrium and obstructive effect of fibroid on uterine vasculature leading to endometrial venule ectasia causing proximal congestion in myometrium and endometrium.[9]

In our study, we evaluated endometrial changes in all the hysterectomy specimens. Of the 826 cases, most showed proliferative endometrium (54.1%), followed by atrophic and secretory endometrium. Endometrial hyperplasia consists of a spectrum of morphologic alterations ranging from benign changes, caused by an abnormal hormonal environment, to premalignant disease.

They are classified by their degree of architectural complexity as simple or complex and by their cytological features as non-atypical or atypical hyperplasia.[14] In our study, endometrial hyperplasia was seen in 3.03% of cases, similar to Rather et al[12] (4.44%). In India, malignancies of uterus are not as frequently encountered as other gynaecological malignancies. In our study, we observed a lower incidence of 0.5%, similar to studies done by Rather et al[12] (0.52%) and Nisa et al[15] (0.69%).

The most common myometrial lesion in our study was leiomyoma (334 cases; 40.4%), similar to study done by Vaidya et al[11] (46.9%). Among the 334 cases of leiomyoma, most (83.2%) were intramural in location and multiple fibroids were seen in 38 cases (11.4%). Velu ARK et al have observed similar findings.[7] In our study, coexistent adenomyosis and leiomyoma were seen in 7.6% cases, similar to studies done by Rather et al[12] (8.02%) and Vaidya et al[11] (8.07%). Raju GC et al[16] have observed in their study that the coexistent leiomyoma and adenomyosis were seen most commonly in the age group of 30-50 years.

In our study, 84.1% of the coexistent cases were seen in the age group of 30-49 years. According to some authors, the reason adenomyosis is common in women aged 35–50 years is because it is the time when women have an excess of oestrogen (oestrogen dominance).[10] Adenomyosis is rarely diagnosed preoperatively due to its vague symptoms. However, radiological modalities like transvaginal ultrasound and MRI are helpful, but the access to these is limited. In our study, adenomyosis was the most common (20.7%) incidental finding, similar to studies done by Jhaet al[17] (17.2%) and Siwatch et al[18] (18.9%). The exact aetio-pathogenesis of adenomyosis is unknown, although various mechanisms and risk factors have been implicated.

Proposed mechanisms include a lack of the basement membrane or the presence of a defect in the membrane at the endomyometrial interface, allowing endometrial tissue to grow into the myometrium. The risk factors hypothesised include hereditary factors, uterine trauma from childbirth or abortion, chronic endometritis, and hyperoestrogenaemia.[10] While correlating the endometrial changes associated with leiomyoma, 22 cases (6.6%) showed atrophic endometrium, similar to study by Velu ARK et al[7] (6.4%). Atrophy may be due to mechanical pressure of the leiomyoma, especially submucous type & large lesions causing thinning of overlying endometrium as well as from postmenopausal hormonal insufficiency.[19]

We also observed 07 cases of endometrial polyps and 12 cases of hyperplasia. Hyperplasia or polyposis may not only be the expression of oestrogenic hyperactivity but also the result of mechanical forces upon the endometrium.[18] Chronic cervicitis is a common condition in adult females; in our study also it was the most common pathology of cervix (98.6%). Rather et al[12] have observed similar findings (89.4%). We also observed 06 cases of invasive carcinoma, similar to Rather et al (04 cases). In our study, 04 cases of CIN of various grade and 01 case of CIS were observed as incidental findings, similar to Siwatch S et al[18] (06 cases of CIN/CIS).

Thus, emphasising the importance of mandatory histopathological examination of all hysterectomy specimens. In the present study, 413 cases were of TAH with UL or BL salpingo-oophorectomy. Most (87.3%) of the ovarian specimens showed physiological changes. In the remaining cases, we observed 51 cases of neoplastic lesions (6.2%), similar to Rather et al (8.02%).[12] However, some authors.[11,17] have reported a higher incidence of ovarian neoplasms. The difference could be explained by our larger sample size. Among the neoplasms, serous cyst adenoma was the most common diagnosis similar to various other studies.[11]

Fallopian tubes are complex structures that represent more than conduits from ovary to endometrial cavity. The significance of pathologic changes in fallopian tubes is related to the possible effect on fertility, exceptions being a few rare tubal neoplasms which may be life threatening. In our study, most of the (91.3%) cases showed normal histology, with the remaining showing hematosalpinx, chronic salpingitis and endometriosis. Rather et al have reported similar findings.[12]

In our study, the correlation of the preoperative diagnosis was seen in 84.8% of cases, which is similar to Siwatch et al[18] (84%). However, 46.5% of the cases showed incidental findings and secondary changes ranging from inflammatory lesions to neoplastic lesions. This could be due to lack of complete documentation in many cases and bias of documentation of preoperative diagnosis wherein the major pathology overshadows the minor ones. Dysfunctional uterine bleeding (DUB), although discarded by FIGO and replaced by AUB, still is widely used for the cases where no systemically or locally definable structural cause of bleeding is observed. We had 38 such cases of which 17 cases were confirmed to be histologically unremarkable. However, in the rest of the cases various incidental findings were noted mostly (47.1%) being adenomyosis. This signifies the need in upgrading of diagnostic services for the diagnosis of adenomyosis.

CONCLUSION: The preoperative diagnosis correlates well with the final histopathological diagnosis. However, there are considerable numbers of incidental findings, which are diagnosed only on histopathological evaluation. Adenomyosis still remains a clinical challenge. Nevertheless, the possibility of this lesion needs to be kept in mind while evaluating the patient. Analysing the preoperative indications for hysterectomy and clinico-pathologic correlation helps recognise malpractice and lacunae in the knowledge or training of health care providers or non-availability of newer alternatives for hysterectomy. Thus, mandatory histopathological evaluation of hysterectomy specimens needs to be practised for diagnostic, quality management and academic reasons.

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