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Unexpected premalignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse

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Abstract

Aim of the study was to estimate the incidence of unexpected premalignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse.

Material and methods: Eighty women with asymptomatic utero-vaginal prolapse were included in this prospective study for vaginal hysterectomy after preoperative preparation and after written informed consent. Women included in this study were screened preoperatively by high vaginal swab, Pap smear, endometrial biopsy and trans-vaginal ultrasound. Surgically removed uteri and ovaries were sent for histopathological examination. Results of histopathological examination as gold standard were compared with conventional gynecological screening methods.

Results: Histopathological examination of surgically removed uteri and ovaries after vaginal hysterectomy for uterovaginal prolapse showed abnormal findings in 61.25% (49/80) of studied cases (10 chronic cervicitis; 20 cervical intra-epithelial neoplasia-1 [CIN-1]; 5 CIN-2; 2 CIN-3; 10 simple endometrial hyperplasia without atypia and 2 simple serous ovarian cyst). Also, histopathological examination showed premalignant changes in 33.75% (27/80) of studied cases (20 CIN-1; 5 CIN-2 and 2 CIN-3), which mean 50% sensitivity of pre-operative Pap smear to detect premalignant cervical changes.

Conclusions: Asymptomatic women with utero-vaginal prolapse may have associated premalignant lesions which may not be detected by conventional screening methods, and this should be explained preoperatively for women undergoing surgery, especially if conservative management was considered.

Key words: unexpected, premalignant, vaginal hysterectomy, utero-vaginal prolapse.

Introduction

Pelvic organ prolapse (POP) is a common health problem, affecting up to 50% of women over 50 years old, with a significant negative influence on the patient's quality of life and daily activity [1, 2].

Vaginal hysterectomy (VH) is the most common surgical procedure for treatment of utero-vaginal prolapse (UVP) [3, 4].

Sacrospinous fixation is a safe and effective alternative to vaginal hysterectomy [2, 3]. There are several proposed conservative methods for management of uterine prolapse such as physiotherapy, electrical therapy and pessaries, but none of them had real evidence for efficacy. Although the use of a pessary has been advocated, it creates some complaints such as vaginal discharge, ulceration, discomfort and dyspareunia. Vaginal hysterectomy still remains the definitive treatment for UVP [5], while Manchester repair, sacrospinous hysteropexy and sacral hysteropexy have been proposed as alternative procedures for women with UVP who desire to preserve their uterus for future pregnancy [6-8]. When conservative uterus-sparing procedure is elected, a thorough and complete preoperative assessment should be done to exclude presence of any precancerous or cancerous pathological conditions of the uterus [3, 9]. Incidence of 0.3-0.8% of unanticipated gynecological cancer in hysterectomy specimens after VH treatment for POP has been reported [3, 10-12].

This study was designed to estimate the incidence of unexpected premalignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse.

Material and methods

Women with asymptomatic UVP admitted to the Sabah Maternity Hospital, Kuwait from January 2008 to

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January 2012 underwent thorough evaluation including history, examination, Pelvic Organ Prolapse Quantification (POPQ) [13, 14], high vaginal swab (HVS), pre-operative Pap smear, trans-vaginal ultrasound (TVS) and endometrial biopsy (done 1-2 weeks pre-operatively).

Women admitted with asymptomatic UVP and concomitant urinary symptoms were also evaluated by urine culture and urodynamic studies. Eighty women with asymptomatic UVP, normal HVS, satisfactory pre-operative Pap smear, and normal pre-operative endometrial biopsy with no uterine or adnexal lesions detected by TVS, without urodynamic abnormalities were included in this study.

Women were included in this study after approval of the institute ethical committee and after informed written consent explaining in detail preoperative assessment, surgical procedure, possible intraoperative and postoperative complications. Women included in this study were evaluated preoperatively for their fitness for anesthesia by a senior anesthetist and underwent preoperative laboratory tests including complete blood count (CBC), renal and liver functions, coagulation profile, electrocardiography (ECG), chest X-ray and cross matched with two units of packed red blood cells (RBCs). Women with a history of endometrial, cervical and/or adnexal precancerous or cancerous pathological conditions, and women presenting with UVP and abnormal uterine bleeding such as menorrhagia or postmenopausal bleeding were excluded from this study. Women on hormonal replacement therapy, postmenopausal women with endometrial thickness ≥ 8 mm or histopathological abnormalities in endometrial biopsy or ovarian or adnexal pathology reported by TVS were also excluded from this study.

Women included in this study were prepared one week before vaginal hysterectomy by vaginal pessary to decrease tissue edema and Betadine vaginal wash to limit as much as possible post-operative infection. Pelvic floor repair and sacrospinous fixation was done to prevent vaginal vault prolapse after VHs. Concomitant cystocele was treated by anterior colporraphy. Both ovaries were removed when accessible vaginally or laparoscopically in the same session of vaginal hysterectomy after closure of the vaginal vault. Specimens were sent for histopathological examination. Results of histopathological examination as gold standard were compared with conventional gynecological screening methods to estimate the incidence of unexpected pre-malignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse.

Sample size justification

Using data from previous studies [15], the required sample size was calculated using G* Power software version 3.17 for sample size calculation (*Heinrich Heine Universität; Düsseldorf; Germany), setting α-error probability at 0.05, power (1-β error probability) at 0.95% and effective sample size (w) at 0.3. The effective size (w) was calculated as follows: $w = \sqrt{\chi^2/N}$, where χ^2 is the χ^2 test and N is the total sample size. The number of participants needed to produce a statistically acceptable figure was 80.

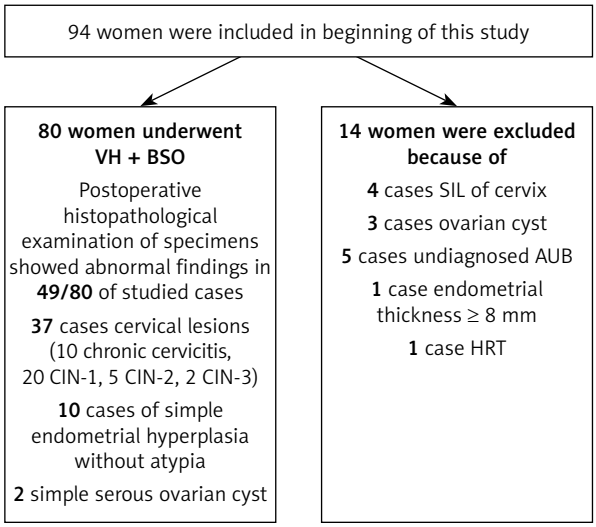
Statistical analysis

Data were collected, tabulated then statistically analyzed using Statistical Package for Social Sciences (SPSS) computer software version 18 (Chicago, IL, USA). Numerical variables are presented as the mean and standard deviation (± SD), while categorical variables are presented as the number (n) and percentage (%). Sensitivity is the proportional detection of individuals with the disease of interest in the population (true positive/true positive + false negative ×100).

Results

Ninety-four women were included at the start of this study. Four women were excluded because of squamous intra-epithelial lesions (SIL) of the cervix, 3 women because of ovarian cyst, 5 women because of undiagnosed abnormal uterine bleeding (AUB), 1 woman because of endometrial thickness ≥ 8 mm, 1 woman because of hormonal replacement therapy (HRT) and 80 women underwent VH and bilateral salpingo-oophorectomy (BSO), pelvic floor repair and sacrospinous fixation (Fig. 1).

Concomitant cystocele was treated by anterior colporraphy in 12 (15%) women. Accessible ovaries were



AUB – abnormal uterine bleeding, BSO – bilateral salpingo-oophorectomy, CIN – cervical intra-epithelial neoplasia, HRT – hormonal replacement, SIL – squamous intra-epithelial lesion, VH – vaginal hysterectomy

Fig. 1. Diagrammatic presentation of study design and results of the study

removed vaginally in 72 (90%) women, while they were inaccessible and removed laparoscopically in 8 (10%) women (Table I).

Mean age of studied women was 58.2 ± 7.99 years, mean body mass index (BMI) was 29.69 ± 5.9 and mean parity was 5.7 ± 2.15, mean operative time was 74.01 ± 16.1 min, mean blood loss was 276.11 ± 171 cc, mean hospital stay was 2.1 ± 0.8 days (Table I).

Four patients received blood transfusion, 1 patient had bladder injury during anterior colporraphy repaired by Vicryl 3/0 in two layers and a silicon catheter was fixed for 5 days. One patient had rectal injury during posterior colpoperineorrhaphy, repaired in two layers by Vicryl 3/0 followed by nothing per mouth (NPO) for 48 hours and neomycin tablets (3 times daily), 1 day fluid diet, 1 day semisolids and finally normal diet.

Histopathological examination of surgically removed uteri and ovaries after VHs for uterovaginal prolapse showed abnormal findings in 61.25% (49/80) of studied cases (10 chronic cervicitis; 20 CIN-1; 5 CIN-2; 2 CIN-3; 10 simple endometrial hyperplasia without atypia and 2 simple serous ovarian cyst). Also, histopathological examination showed premalignant changes in 33.75% (27/80) of studied cases (20 CIN-1; 5 CIN-2 and 2 CIN-3), which means 50% sensitivity of pre-operative Pap smear to detect premalignant cervical changes (Fig. 1 and Table II).

Discussion

Eighty women were included in this prospective study to estimate incidence of unexpected premalignant gynecological lesions in women undergoing vaginal hysterectomy for UVP. All women included in this prospective study presented with asymptomatic UVP with negative pre-operative diagnostic workup including HVS, Pap smear, TVS and endometrial biopsy.

The incidence of unanticipated endometrial malignant and premalignant lesions in the literature among asymptomatic women with UVP undergoing hysterectomy for POP varies between 0.7 and 2.6% [10-12].

In this study 10 (12.5%) cases of simple endometrial hyperplasia without atypia and no cases of premalignant endometrial lesions were detected by postoperative histopathological examination of surgically removed uteri. This can be explained by the exclusion criteria of this study, which excluded postmenopausal women with endometrial thickness ≥ 8 mm and women with abnormal endometrial biopsy. Also, this low incidence of premalignant endometrial lesions in this study confirms the accuracy of TVS as a screening tool in detection of thickened endometrium which necessitates endometrial biopsy.

Renganathan *et al*., in a retrospective study, found that among 517 asymptomatic women without AUB who underwent hysterectomy for POP, 4 (0.8%) women had unexpected endometrial carcinoma. Renganathan *et al*. concluded that a preoperative TVS should be performed in all cases, followed by endometrial sampling in women with thickened endometrium [10].

Frick *et al*. in a retrospective study found that 0.2% of asymptomatic postmenopausal (1/421) and 0% (0/115) of 115 premenopausal women had endometrial carcinoma, and 2.6% (11/421) of asymptomatic postmenopausal women had endometrial cancer or hyperplasia. Frick *et al*. concluded that although the risk of missing a malignancy is low, this low risk can be further reduced by routine preoperative endometrial biopsy and/or TVS [11].

Wan *et al*. found 0.7% (3/456) of endometrial premalignant lesions among asymptomatic women, and this lower incidence was explained by low prevalence of endometrial cancer in the Asian population [12].

Smith-Bindman *et al*. concluded that in asymptomatic postmenopausal women with an endometrial

Tab. I. Characteristics of the studied women with utero-vaginal prolapse

Variables	Total of 80 studied women
Age (years); mean ± SD	58.2 ± 7.99
Body mass index (BMI) (kg/m^2), mean ± SD	29.69 ± 5.9
Parity, mean ± SD	5.7 ± 2.15
Operative time (minutes), mean ± SD	74.01 ± 16.1
Concomitant cystocele, number (%)	12 (15%)
Laparoscopic bilateral salpingo-oophorectomy (BSO), number (%)	8 (10%)
Intra-operative blood loss (cc), mean ± SD	276.11 ± 171
Hospital stay (days), mean ± SD	2.1 ± 0.8

Tab. II. Histopathological findings not detected by conventional gynecological screening methods

Histological findings	Total cases not detected by conventional screening (49 cases)
Chronic cervicitis, number (%)	10 (12.5)
Cervical intra-epithelial neoplasia-1 (CIN-1), number (%)	20 (25)
Cervical intra-epithelial neoplasia-2 (CIN-2), number (%)	5 (6.25)
Cervical intra-epithelial neoplasia-3 (CIN-3), number (%)	2 (2.5)
Simple endometrial hyperplasia without atypia, number (%)	10 (12.5)
Ovarian cyst, number (%)	2 (2.2)

thickness of ≥ 11 mm an endometrial biopsy should be performed, while others used cut-off values of endometrial thickness in asymptomatic postmenopausal women of 3-10 mm [16, 17].

Menon *et al*., in a classic retrospective study of 170 women, concluded that the likelihood of progression from endometrial hyperplasia to carcinoma was found to be between 1% in cases of simple hyperplasia without atypia and 29% in cases of complex atypical hyperplasia [15].

Menon *et al*. reported that no cases of ovarian cancer and only 3 cases of small serous cysts were detected by TVS among 86 women who underwent BSO, without any clinical consequences. Menon *et al*. explained these results by the excellent specificity and negative predictive value of TVS in detection of ovarian lesions before BSO [15].

All women included in this study had normal ovarian morphology and were negative for any ovarian pathology by TVS, while postoperative examination of ovaries showed 2 (2.5%) simple serous ovarian cysts. This reflects the importance of preoperative TVS for asymptomatic women undergoing VHs for detection of any ovarian lesions. It also reflects the importance of preoperative counseling of patients about difficulties of removal of enlarged ovaries during VHs which may necessitate a laparoscopic procedure to remove enlarged ovaries [18].

In this study, histopathological examination showed premalignant changes in 33.75% (27/80) of studied cases (20 CIN-1; 5 CIN-2 and 2 CIN-3), which reflects moderate sensitivity (50%) of pre-operative Pap smear in detection of premalignant cervical changes in our laboratory. Cuzick *et al*. found one case (0.3%) of cervical cancer in a 71-year-old patient who had negative smear tests 14 months before surgery and one case (0.3%) of CIN-3 in a 66-year-old patient with normal smear test results 3 years before surgery and 3 cases of CIN-1 with normal smear tests 6 months to 3 years before surgery [18].

Refusal of women to participate in this study and absence of a consensus about cut-off values of endometrial thickness in asymptomatic postmenopausal women requiring subsequent endometrial biopsy were limitations of this study.

Based on this study, we conclude that asymptomatic women with utero-vaginal prolapse may have associated premalignant lesions which may not be detected by conventional screening methods, and this should be explained preoperatively for women undergoing surgery, especially if conservative management was considered.

Disclosure

Authors report no conflict of interest.

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