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CONSISTENCY OF ENDOMETRIAL SAMPLING WITH SUBSEQUENT HYSTERECTOMY FINDINGS IN DUHOK-IRAQ

[1]Kawar Sardar Abdulkareem, [2]Alaa Hani Raziq

ABSTRACT*-Endometrial sampling is one of the commonest diagnostic procedures and upon its results various actions will be set. This study aimed to compare the results of endometrial biopsy and proceeding hysterectomy and to determine the value of endometrial biopsy in the diagnosis of various pathologies. This study is a comparative one between the results of endometrial sampling and hysterectomy and included 200 patients from 1-1-2012 until 1-1-2018 in Duhok City-Iraq. Pregnancy related disorders were excluded. Histological reports and slides were retrieved from the bank of data in the central laboratory of Duhok City. Results of both procedures were put in three categories; the non-significant differences, the significant and consistent findings and the significant and inconsistent results. The reliability of endometrial biopsy was determined for carcinoma and hyperplasia. In addition, upgrading and downgrading of certain disorders was calculated. For the significant and inconsistent category, intra and inter-observer variability were estimated. The age of the included patients ranged from 27-80 years with a mean of 53.5 years ± (26.5). There were non-significant differences in (53%) of cases, significant and consistent results in 9% of cases and significant but inconsistent results in 38% of cases. In the latter group the intra-observer and inter-observer variabilities were (22.4%) and (77.6%) respectively. For carcinoma cases, endometrial sampling was reliable in (100%) of cases but for hyperplasia, correct diagnosis was given in only 30.8% of cases. Significant and inconsistent results of endometrial biopsy when compared to hysterectomy were found in (38%) cases a finding should make the gynecologists deal with awareness when making a proceeding decision to utilize other investigations modalities in conjunction. Regarding endometrial carcinoma, endometrial sampling is a reliable diagnostic procedure but this reliability is diminished for other pathologies.*

Keywords- *Endometrium, carcinoma, hyperplasia, upgrading, downgrading, hysterectomy*

I INTRODUCTION

The dynamicity of the endometrium is influenced by hormonal, stromal and vascular factors aiming to embryo implantation and supporting the nutritional needs of the subsequent pregnancy. Estrogen is a potent stimulator for proliferation of the endometrium whereas progesterone secreted by the corpus luteum after ovulation suppresses proliferation and initiates secretory status. Failure of conception creates hormonal withdrawal leading to endometrial breakdown and menses (Landrum, Zuna, & Walker, 2018). Endometrial sampling represents one of the most common day-to-day surgical pathological specimens and probably the most common one (Longacre, Atkins, Kempson, & Hendrickson, 2010). Diagnostic specimens are obtained through the traditional procedure of

[1] *M.B.Ch.B., Directory of Health/Duhok*
[2] *F.I.C.M.SUniversity of Duhok, College of Medicine, Pathology Department*

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dilation and curettage (D&C) and ideally it should involve excision of the entire or near entire uterine mucosa (Gilks, 2017) (Mills & E., 2007). Indications of D&C include; abnormal uterine bleeding, cancer screening, and workup for infertility (Longacre, Atkins, Kempson, & Hendrickson, 2010). The procedure can be done blindly or with the aid of hysteroscopy. Endometrial sampling is simple to perform and should be considered of value only when positive for malignancy. In atypical hyperplasia, evaluation of the whole endometrium is necessary to rule out carcinoma. Rarely annual screening by endometrial sampling is indicated for example in women older than 35 years old, with Lynch syndrome and/or a family history of carrying the mutation (Gonçalves & Anschau, 2016). The value of endometrial biopsy is unquestionable in postmenopausal bleeding and irregular bleedings premenopausally (Soliman & Lu, 2017). An exceptional event is the failure to demonstrate a tumor in hysterectomy specimen after its demonstration in endometrial biopsy. This distressing event, which has been referred to as vanishing endometrial carcinoma (This event is also described in the prostate) can be explained by the very minute size of the tumor, most or all of which had been removed by the previous biopsy (Gilks, 2017). The procedure requires anesthesia, and there is a small but definite risk of uterine perforation or secondary amenorrhea resulting from post-curettage adhesions (Asherman syndrome) (Longacre, Atkins, Kempson, & Hendrickson, 2010).

Hysterectomy is one of the most common surgical procedures and ranks second only to cesarean section (Stovall, 2007). The vast majority of hysterectomies are done to alleviate the symptoms of pain, bleeding, or both in common diseases which are either benign conditions (Uterine leiomyomas, excessive menstrual bleeding, pelvic organ prolapse, endometriosis, adenomyosis, pelvic inflammatory disease, Chronic pelvic pain, dysmenorrhea, obstetric indications, cervical intraepithelial neoplasia (CIN), atypical endometrial hyperplasia) or malignant conditions (Cervical cancer, endometrial cancer, fallopian tube cancer , ovarian cancer, gestational trophoblastic tumors, rectal or bladder cancer with uterine involvement). Hysterectomy can be performed vaginally, abdominally, or with laparoscopic assistance (Barber, 2007). “Simple” – as opposed to radical – hysterectomy and bilateral salpingo-oophorectomy remains the cornerstone for the treatment of endometrial cancer. There is a trend toward a reduction of radicality in micro invasive or low-volume early cervical cancer which put simple hysterectomy in the armamentarium for the surgical management of cervical cancer. Total hysterectomy is usually performed through an open approach to facilitate complete assessment of the peritoneal cavity and the lymph node status (Querleu, Plante, Sonoda, Gotlieb, & Leblanc, 2013). The type of hysterectomy (total or radical) and the disease (benign or malignant) determine the method for processing the specimen. Specimens fall into three categories: total hysterectomies for benign conditions (e.g., prolapse or fibroids), total hysterectomies for malignant conditions (e.g., endometrial carcinoma) and radical hysterectomies for malignant conditions (e.g., cervical carcinoma) that include vaginal cuff, parametrium, and regional lymph nodes (French & Curtis, 2010). Radical hysterectomy with en bloc total vaginectomy is rarely performed in gynecologic oncology (Cibula, 2015). The aims of this study are to test the reliability of endometrial sampling against hysterectomy and to find intra and inter observer’s variability for inconsistent results.

II METHODS

This study includes 200 patients in a period of 6 years from 1-1-2012 to 1-1-2018 who underwent both endometrial biopsy and hysterectomy. Reports and slides were retrieved from central laboratory in Duhok City and each patient was given a code to secure the privacy of the patients as well as signing pathologists.

Patients were grouped according to their ages with a 10 years interval for each group.
Histopathological reports of endometrial biopsy sampling and hysterectomy were reviewed and comparison between the results done.

For hysterectomy specimens, patients were grouped into those with endometrial pathology, those with non-endometrial pathology and both. And for those with endometrial pathology the results were compared to the pre-hysterectomy endometrial sampling result. After that the differences in findings were classified into three categories; the first category when there were non-significant differences (that were related to phase difference or effect of hormonal therapy), the second category when there were consistent and significant findings and the third category when the results are significant but inconsistent here the inter and intra-observer variability was estimated.

III RESULTS

This study included 200 patients who underwent endometrial sampling followed by hysterectomy. The youngest patient was 27 years old and the oldest was 80 years old with a mean of 53.5 ± (26.5) and (59%) were in the age group between 41-50 years. The age group of the included patients is shown in figure (1). Regarding endometrial biopsy results, 13 patients had hyperplasia and 12 patients had carcinoma and all the results are shown in table 1. The results of hysterectomy specimens were divided into three groups; those with endometrial findings, those with non-endometrial pathology and those with both. Endometrial findings included 13 patients with endometrial adenocarcinoma and only 4 patients with hyperplasia. Table 2, 3, 4 summarize the findings in hysterectomy specimens.

There were non-significant findings in 107 patients (53%) and in 17 patients (9%) results of endometrial biopsies and that of hysterectomy were significant and consistent while in 76 patients (38%) the results were significant but inconsistent. For the last group 17 cases out of 76 cases were signed by the same pathologist giving rates of (22.4%) intra-observer variability and (77.6%) inter-observer variability.

The histopathological findings in endometrial biopsies were upgraded in 35 patients out of the included 200 patients and downgraded in 15 patients representing (17.5%) and (7.5%) respectively.

Regarding endometrial carcinoma, it was diagnosed in 12 patients by endometrial biopsy and in 13 patients of hysterectomy and if we exclude the only one patient because of the wide time interval between the two procedures which was 5 years we will get a (100%) reliability of endometrial biopsy compared with the results of hysterectomy. While hyperplasia was diagnosed in 13 patients by endometrial biopsy and was proved in only 4 patients of these 13 (30.8%).

Upgrading of the histological finding by endometrial biopsy was detected in 35 cases (17.5%) and downgrading in 17 cases (7.5%).

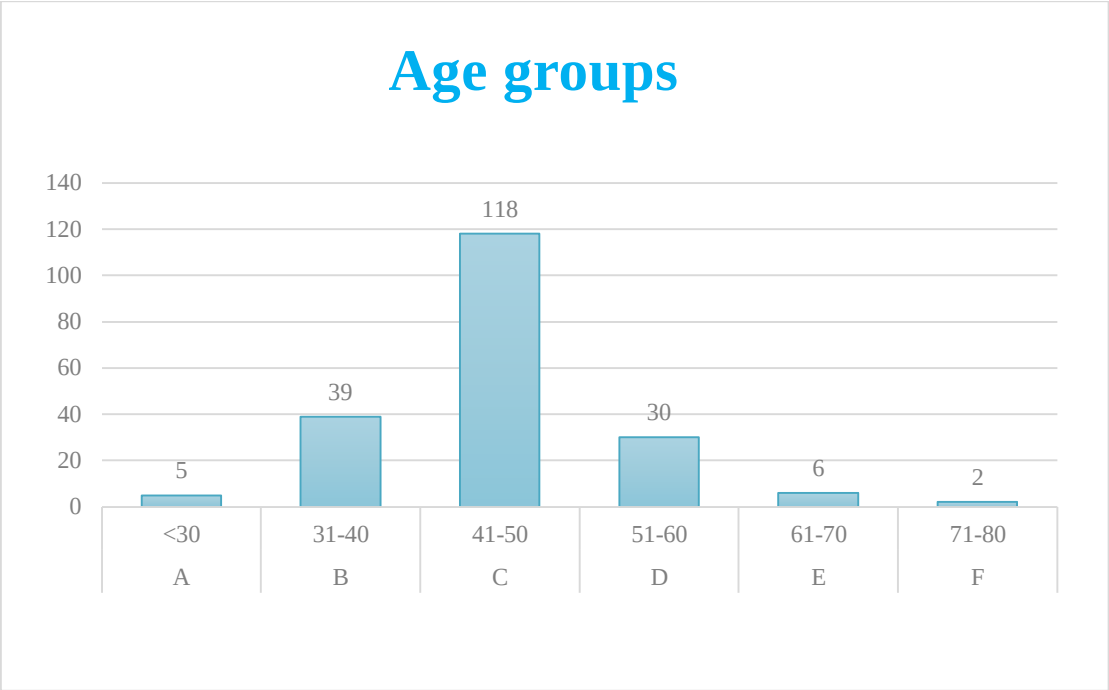

Figure 1: The age distribution of the enrolled patients

Table 1: Histopathological findings in endometrial biopsies

Histopathology	No.	%
Secretory phase	68	34%
Proliferative phase	40	20%
Menstrual phase	10	5%
Disordered proliferative	28	12.5%
Inactive endometrium	13	6.5%
Polyp	8	4%
Endometritis	6	3%
Atrophic	2	1%
Hyperplasia	13	6.5%
Endometrial carcinoma	12	6%
Total	200	100%

Table 2: Endometrial findings in hysterectomy specimens

Findings	NO.	%
Secretory phase	48	24%
Proliferative phase	69	34.5%
Disordered proliferative	19	9.5%
Inactive endometrium	10	5%
Polyp	19	9.5%
Endometritis	4	2%
Atrophic	14	7%
Hyperplasia	4	2%
Carcinoma	13	6.5%
Total	200	100%

Table 3: Non- Endometrial findings in hysterectomy specimens

Non-endometrial findings	No.	%
Adenomyosis	**59**	**29.5%**
Leiomyoma	**35**	**17.5%**
Adenomyosis and leiomyoma	**6**	**3%**
Fibroma thecoma	**2**	**1%**
Dysplasia of cervix	**3**	**1.5%**
Teratoma	**1**	**0.5%**
Granulosa cell tumor	**1**	**0.5%**
No pathology	**93**	**46.5%**
Total	**200**	**100**

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Table 4: Cases with both endometrial and non-endometrial pathology

Both	No.	%
Atrophic endometrium and leiomyoma	8	4%
Atrophic endometrium and adenomyosis	4	2%
Atrophic endometrium and fibroma-thecoma	1	0.5%
Atrophic endometrium and adenomyosis&liomyoma	1	0.5%
Hyperplasia and lioemyoma	2	1%
Hypeplasia and adenomyosis	1	0.5%
Endometritis and fibroma	1	0.5%
Disordered proliferative and leiomyoma	4	2%
Disordered proliferative and adenomyosis	5	2.5%
Disordered proliferative, adenomyosis and leiomyoma	1	0.5%
Inactive endometrium and adenomyosis	3	1.5%
Inactive endometrium and leiomyoma	2	1%
Inactive endometrium, adenomyosis and leiomyoma	1	0.5%
Inactive endometrium, leiomyoma and cervical dysplasia	1	0.5%
Total	35	17.5%

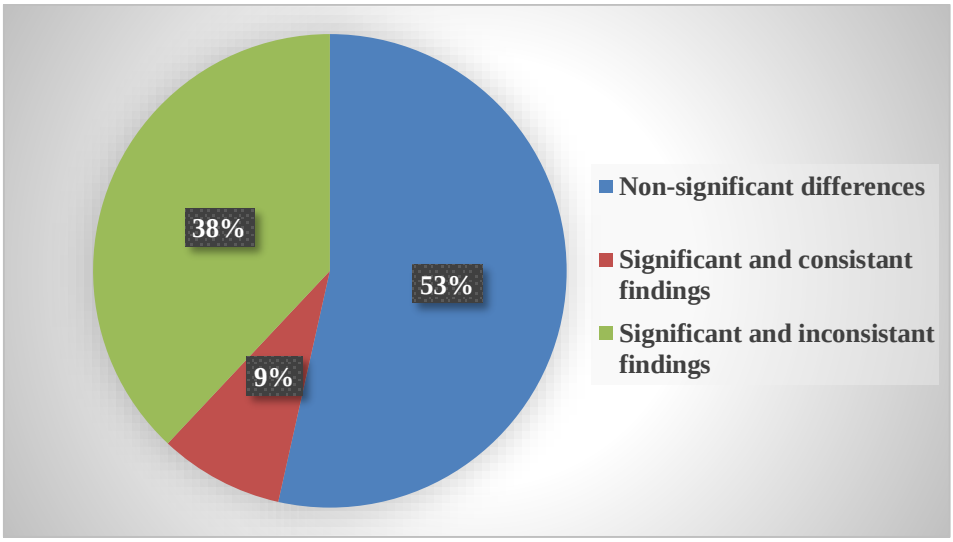

Figure 2: Comparison of results of endometrial biopsy and hysterectomy

Table 5: Up graded histopathological findings by endometrial biopsy

Endometrial biopsy	Hysterectomy	Upgraded	Percentage
23 Disordered proliferative	13proliferative phase, 4secretory phase, 4atrophic and 2inactive	23	65.7%

11 hyperplasia	3 proliferative phase, 4 secretory phase, 3 Disordered proliferative and 1atrophic	11	31.4%
1 carcinoma	1 complex hyperplasia	1	2.9%
Total		35	100%

Table 6: Downgraded histopathological findings by endometrial biopsy.

Endometrial biopsy	Hysterectomy	Down graded	Percentage
5secretory phase	1 carcinoma , 4disordered proliferative	5	33.3%
3 proliferative phase	1carcinoma, 1 hyperplasia and 1disordered proliferative	3	20.1%
5 menstrual phase	5 disordered proliferative	5	33.3%
2 inactive endometrium	2 diordered proliferative	2	13.3%
Total		15	100%

IV DISCUSSION

Endometrial biopsy is the most common procedure in gynecology (Longacre, Atkins, Kempson, & Hendrickson, 2010), and upon its results various decisions are taken which not uncommonly will be a hysterectomy (Wieslander & Wong, 2013). The differences between histopathological results of endometrial sampling and hysterectomy may be attributed to many factors. One of the important contributory factors is the limited sample in endometrial biopsy versus the complete specimen of hysterectomy. In addition to the time difference between the two procedures and the effects of prior hormonal therapy. Added to these factors is the intra and inter observer variability.

In this study significant and inconsistent results were obtained in (38%) of cases while in one study performed by Sinha et al (2011), they found a non-concordance in (49%) of their cases. In another study limited to cases of hyperplasia, the consistency rate between the two procedures was only (41.3%) and in our study the reliability of endometrial biopsy for cases of hyperplasia was only (30.8%) (Sinha, ReKha, KonaPuR, Selvi, & SuBRamaniam, 2011). Probably this is related to the different schemes in the classification of hyperplasia and to the fact that subjectivity and over-estimation may play a role in the diagnosis of hyperplasia.

For malignant cases, if we exclude the only one patient with the five year interval between the two procedures, the reliability of endometrial biopsy is (100%) and this is clearly related to the fact that the diagnosis of malignancy is clear and obvious to the pathologists because of the cytological and architectural atypia associated with malignant changes. Huang et al (2007) studied the sensitivity of endometrial biopsy for cancer cases by grade and it was (95.2%) for low grade and (99.3%) for high grade carcinomas (Huang, et al., 2007). Dis-concordance,

upgrading and down grading was also observed by other investigators (Wang X et al 2005) (Wang, Huang, Di, & Lin, 2005).

Barut A and coworkers reported accuracy of (99.5%) and (96.8%) for malignant pathologies diagnosed from curettage material for pre- and postmenopausal women, respectively (Barut, et al., 2012).

In this study, the histopathological findings of endometrial biopsy were upgraded in 35 cases (17.5%) and downgraded in 15 cases (7.5%). Sinha P et al (2011) reported an upgrading in 19 patients and downgrading of 16 patients out of their cases which were 131 cases (Sinha, ReKha, KonaPuR, Selvi, & SuBRamaniam, 2011).
Dis-concordance in the diagnoses of disordered proliferative endometrium, hyperplasia and endometritis may be explained by the abundance of tissue in hysterectomy in addition to subjectivity related to inter-observer variability.

V CONCLUSION

The finding of significant and inconsistent results of endometrial biopsy when compared to hysterectomy in (38%) of cases necessitate increasing awareness from the gynecologist to consider other parameters (clinical and imaging) together with the histopathological results of endometrial biopsy in dealing with patients with abnormal uterine bleeding. In addition, endometrial sampling is a reliable diagnostic procedure for endometrial adenocarcinoma but limited in cases of hyperplasia.

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