Incidence and Cytomorphological Peculiarities of Lower Genital Tract Infections in Vault (Post Hysterectomy) Smears Versus Pap Smears from Non-Hysterectomy Subjects: A Retrospective Study

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Abstracts

Objective To evaluate morphology and frequency of lower genital infections in (post hysterectomy) vault smears of women.

Methods We analyzed vault smears from 500 women who had undergone hysterectomy, either for benign diseases (230) or for carcinoma cervix (270) and findings were compared with Pap smear diagnosis of non-hysterectomy subjects.

Results Majority 432/500 (87%) of the vault smears were negative for squamous abnormality in comparison to 381/500 (76%) Pap smears from non-hysterectomy subjects. It was observed that 48 (9.6%) vault smears showed lower genital tract infections, however frequency of infections was reported significantly higher 101 (20.2%) in non-hysterectomy subjects. *Gardenerella vaginalis* was the leading infection in vault smears 26 (5.2%) due to benign diseases and was prevalent in the fifth and sixth decades of life of women in comparison to 43 (8.2%) in Pap smears with higher prevalence in the fourth decade of life. *Trichomonas vaginalis* and Human Papillomavirus infection were the second commonest infections in vault smears followed by *Candida albicans*. **Conclusion** Cytologically diagnosed gynecological infections were remarkably low 48 (9.6%) in vault smears as

compared to 101/500 (20.2%) amongst non-hysterectomy subjects. Infections which mainly thrive at the Squamocolumnar junction i.e. HPV, Chlamydia and HSV were absent or rare in vault smears. Further incidence of infections in the vault smears where hysterectomy was done due to carcinoma cervix was as low as 10 (3.7%) as compared to 38 (16.5%) where hysterectomy was done due to benign uterine diseases.

Keywords Post hysterectomy · Cervical infections · Vault smears

Introduction

The Papanicolaou smear was originally designed to detect malignant cervical lesions, subsequently used to diagnose not only cancerous lesions but precancerous lesions and other lower genital tract infections of the uterine cervix including human papilloma virus infection [1]. Cytology is widely used as a rapid, cost effective, non-invasive technique in the evaluation and follow up of patients subjected for hysterectomies [2]. It is estimated that by the age of 60 years approximately 30% women undergo hysterectomy; approximately 85% of these hysterectomies are performed for benign diseases and 15% for carcinoma cervix [3]. Any recurrence of carcinoma after treatment can be detected by smearing the vault periodically and managing the patients accordingly, likewise in case of hysterectomy done due to benign condition, status of vault can be reflected by

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collecting smears [4]. It is not possible to predict the outcome of treatment on clinical grounds alone and the routine vault smear, during follow up visit, is almost mandatory for women who have undergone hysterectomies for any reason. Even the examination of Pap smears during and after radiotherapy/chemotherapy offers a more precise determination of the response of the individual patients [5, 6]. There is enough literature on the efficacy of vaginal cuff testing [4, 7] but little information is available on the frequency of lower genital tract infections in follow up cytologic examination after hysterectomy. We therefore performed a retrospective study of 500 vault smears to evaluate cytologic findings in relation to cervical infections in women undergone hysterectomy due to any reason (benign diseases or cancer cervix) and at any age with the corresponding cervical Pap smears from non-hysterectomy subjects.

Material and Methods

The Papanicolaou stained vault smears of 500 women, who underwent hysterectomies due to benign gynecologic diseases (230) or due to carcinoma cervix (270) were reviewed and analyzed to predict the risk of squamous abnormality and specifically the frequency of lower genital infections. For meaningful comparison same number of cervical Pap smears from non-hysterectomy subjects attending Gynae OPD of Lok Nayak hospital of Delhi were also reviewed. The details of patient's age at the time of hysterectomy, clinical diagnosis, reason for hysterectomy were also recorded and described in Table 1.

Results

The mean age of 230 patients at the time of hysterectomy for benign uterine conditions was 41 years (median 48 years) with a range of 23–62 years and mean age of the 270 patients at the time of hysterectomy for carcinoma cervix was 50 years (median-50 years) with a range of 21–70 years. For this study all the subjects were categorized into five categories as/decades of life (21–30, 31–40,

41–50, 51–60, 61–70 years). Benign uterine diseases were found prevalent in fifth decades of life in 105/230 (45.6%) followed by fourth decades in 71 (30.8%) women. Fibroid uterus 135/230 (58.6%) was the most common indication for hysterectomy, followed by Dysfunctional Uterine Bleeding 55 (23.9%) and prolapse uterus 40 (17.3%). Incidence of cancer cervix was also found prevalent in the fifth decade of life 115 (42.5%) followed by fourth decade 70 (25.9%) and then sixth decade 53 (19.6%) of life. The age wise prevalence and indications for hysterectomies are given in Table 1.

Majority of vault smears 437 (87%) were negative for any squamous abnormality and were either normal 300 (60%) or inflammatory 137 (27%) however Pap smears from non-hysterectomy subjects showed reverse findings where 150 (30%) smears were normal and 231 (46%) inflammatory. The lower genital tract infections which included *Gardnerella vaginalis* (GV), Human Papilloma-virus (HPV), *Trichomonas vaginalis* (TV), *Candida* were reported in 48 (9.6%) vault smears, however infections of Herpes Simplex virus (HSV) and Chlamydia were not detected cytomorphologically. Infections including Chlamydia and HSV accounted for 98 (19.6%) in non-hysterectomy subjects during routine screening programme, the incidence being more than double the test group. Low incidence of infection in vault smears was obvious even though the women were in sexually active decades of life. Incidence of infection in the vault smears where hysterectomy was done due to carcinoma cervix was as low as 10/270 (3.7%) as compared to 38/230 (16.5%) where hysterectomy was done due to benign uterine diseases. The infection of GV were seen in 26 (5.2%) vault smears as compared to 43 (8.6%) from routine Pap smear. In non-hysterectomy subject the Pap smears showed blue colored short rods tending to accumulate on the surface of epithelial cells, concentration being more on the margin thus blurring the cell margins. These cells are commonly known as “Clue cells”. Fine granular material gave overall dirty appearance of the smear. In vault smears clue cells were present in small number and smears were cleaner as compared to non-hysterectomy subjects. The infection of TV was prevalent in the sexually active phase of life of

Table 1 Age wise prevalence and cause (benign and malignant indications) of hysterectomy in study women

Status of women	Age at hysterectomy	Benign uterine diseases			Carcinoma cervix	Total
		Fibroid	DUB	Prolapse		
Premenopausal	21–30	10	9	4	12	35
	31–40	45	18	8	70	141
	41–50	60	25	20	115	220
Postmenopausal	51–60	15	3	8	53	79
	61–70	5	–	–	20	25
Total		135	55	40	270	500

women i.e. 21–50 years irrespective of reason for hysterectomy. In vault smears TV appeared as small grey green round or elliptical structures with eccentric nuclei without much cellular changes while cells in Pap smear from non-hysterectomy subjects showed cytoplasmic eosinophilia, perinuclear halos, and excessive cytolysis. The infection of HPV was reported in 8 (1.6%) vault smears however incidence was three fold higher 24 (4.8%) in non-hysterectomy subjects. The HPV infection induces cytomorphological changes in cervical epithelium in two forms: first classical changes reflects formation of koilocytes i.e. epithelial squamous cells with cytoplasmic condensation at the periphery with large paranuclear halo and eccentrically placed dark nucleus, and second non-classical changes where full blown koilocytes are not formed but features of rounding of cells with cytoplasmic condensation and eccentric/hanging nuclei are seen. Cells are seen in sheets and chords. In vault smear we could see few round cells in small clusters with thickening of borders, cytoplasmic vacuolation and eccentric nuclei depicting only non-classical category of HPV induced changes while cells in Pap smears from non-hysterectomy subjects showed classical as well as non-classical changes of HPV infection. Infection of *Candida* was reported in 4 (0.8%) vault smears but frequency was four times higher as 12 (2.4%) in non-hysterectomy subjects. Infection of HSV and Chlamydia were totally absent in vault smears while observed in few Pap smears from non-hysterectomy subjects. No more than one infection at a time was seen in the vault smears and there was no low grade or high grade lesions seen in vault smears of women subjected for hysterectomy. Non-hysterectomy subjects showed 0.6% Atypical Squamous cells (ASC), 0.8% each LSIL-Mild dysplasia or HSIL. Malignant cells were only seen in the 15/500 (3%) vault smears of women who underwent hysterectomy for carcinoma cervix on follow up indicating recurrence. Age wise prevalence of infection and squamous abnormalities in vault smears versus non-hysterectomy subjects are described in Table 2.

On comparing the diagnosis of vault smears due to benign diseases versus due to carcinoma cervix it was

observed that lower genital tract infections (including HPV) were frequently seen in 38 (16.5%) vault smears of women subjected for hysterectomy due to benign gynecologic diseases in comparison to 10 (3.7%) vault smears due to carcinoma cervix. Vault smears after hysterectomy for benign uterine diseases showed infection of GV four time higher, HPV three time higher and TV two time higher when compared with vault smears after hysterectomy for carcinoma cervix. No infection of *Candida*, HSV and chlamydia was seen after hysterectomy for carcinoma cervix. No squamous abnormality was reported after hysterectomy for benign diseases Table 3.

Discussion

The lower genital tract infections of the uterine cervix are closely related with age, marital status, promiscuity, socioeconomic status, malnutrition and genital hygiene. High incidence of infections in general is also attributed by the lowered immune status of the females due to varied physiological conditions of the body like diabetes and AIDS. Hygiene of the lower genital tract is directly related to the infections and inflammation of genital organs of female [8]. In developing countries where hygiene is poor incidence of infections is generally high as compared to developed countries [9].

We investigated the frequency of lower genital tract infections in vault smears of women subjected for hysterectomy due to any reason in her past and it was observed that 48 (9.6%) vault smears showed infections of GV, HPV, TV and *Candida*, however these infections were accounted for 101 (20.2%) in normal women during routine screening programme as reported earlier also [10, 11]. The reason is related to sexual activity of women. After hysterectomy every women reacts differently, and reactions are a combination of emotional and physical responses. Some women enjoy sex more after hysterectomy, particularly if they had a lot of bleeding and pain before surgery. Some women feel more relaxed not worrying about getting pregnant. Infection

Table 2 Age wise prevalence of cytologic diagnosis and infections of vault smears after hysterectomy/Pap smears from non-hysterectomy subjects

Age	Normal No./%	Inflammation	GV	TV	HPV	Candida	HSV	Chla mydia	ASC	LSIL (mild dysp.)	HSIL	Ca	Total
21–30	13/40	5/56	5/0	2/2	0/5	0/2	–	0/2	0/2	0/2	–	–	25/112
31–40	51/63	27/70	2/30	3/5	2/10	3/5	0/3	–	0/1	–	–	1/0	89/187
41–50	120/30	45/71	10/10	5/7	6/7	1/3	–	–	–	0/2	0/1	2/2	189/133
51–60	70/10	24/25	9/3	0/0	0/2	0/2	–	–	–	–	0/3	5/2	108/47
61–70	46/7	36/10	–	–	–	–	–	–	–	–	–	7/4	89/21
Total%	300/150	137/231	26/43	10/14	8/24	4/12	0/3	0/2	0/3	0/4	0/4	15/8	500/500
	60/30	27.4/462	5.2/8.6	2/2.8	1.6/4.8	0.8/2.4	0/0.6	0.04	0/0.6	0/0.8	0/0.8	3/1.6	

Table 3 Age wise prevalence of cytologic diagnosis of infections in vault smears due to benign uterine diseases/carcinoma cervix

Age	Normal	Inf	GV	TV	HPV	Candida	Abnormal	Total
21–30	8/2	–	4/1	2/0	–	–	–	16/3
31–40	27/29	18/10	2/0	0/2	0/2	3/0	0/1	53/44
41–50	50/80	21/35	8/2	5/1	6/0	1/0	0/2	91/120
51–60	35/35	14/20	7/2	–	–	–	0/5	56/62
61–70	10/25	4/9	0/0	–	–	–	0/7	14/41
Total	130/171	57/74	21/5	7/3	6/2	4/0	0/15	230/270

like HSV, chlamydia and HPV which are more common in sexually active decades of life were absent or rare in vault smears in comparison to non-hysterectomy subjects. These infections grow by infecting delicate endocervical epithelium in endocervical canal at the place of squamo-columnar junction and after hysterectomy, by removal of cervix *utero-viz-a-viz* squamo-columnar junction; there are little chances of these infections. The GV was the leading infection associated with inflammation and infected 21/230 (9.1%) women after hysterectomy for benign diseases and more prevalent in the age group of 41–50 years while cancer patients showed only 5/270 (1.8%) cases having GV infection. The higher prevalence of GV as post hysterectomy infection was also reported by Kristiansen et al. [12]. This difference in frequency rate of GV with and without hysterectomy inflammation is highly significant and suggests a causative role of organism. The morphological peculiarities of GV were different in vault smears with less number of clue cells. The cellular changes, cytoplasmic eosinophilia, perinuclear halos, and excessive cytolysis, induced by infestation of TV were not seen in vault smears however organism seen adjacent to the cells as well as in the background. The frequency of HPV infection was reported in 8/230 vault smears but it was reported in few vault smears 3/220 by Videlefsky et al. [4]. As well as classical changes of HPV infection like koilocyte formation, large perinuclear halo and large hyperchromatic nuclei were not found in vault smears after hysterectomy, however cytoplasmic condensation and eccentric/hanging nuclei were supporting features for the diagnosis of HPV infection and they proved for the positivity of HPV DNA and HPV types 16 also. Gynecologic infections as well as dysplastic lesions, in vaginal cuff testing after hysterectomy for benign uterine diseases, also reported by Videlefsky et al. [4] but incidence was much higher in comparison to present results and in present study no squamous abnormality was detected in vault smears due to benign uterine conditions. The low rate of infection in women aging 51–60 years and above may be explained on the basis that women by the age of 50 years reached to the menopausal status of life and are less sexually active which was a supporting factor towards lesser rate of infection. The present study revealed the importance of follow up cytologic examination after hysterectomy as it is observed that lower genital tract infections occur mainly in premenopausal age of

women when the women are usually sexually active irrespective of their hysterectomy for benign diseases and frequency of infections decreased as the normal women gets older. It is concluded from the results that examination of vault smears after hysterectomy due to benign diseases or cancer is important to know the status of vault in relation to gynecologic infections as well as for detection of any abnormality in the vault. More significantly HPV, chlamydia and HSV infections were absent or rare in vault smear irrespective of any decade of life simply because of the fact that squamo-columnar junction, site of infection, was no more in hysterectomy cases which is must for initiation and proliferation of these infections.

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