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Clinicopathological Study of Tumours and Tumour Like Lesions of The Uterine Cervix

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Abstract
Background: Cervical cancer is the most common cancer of female genital tract in India. The present study was undertaken to analyze the spectrum and incidence of various tumour and tumour like lesions of uterine cervix and study the relation with clinical and pathological characteristics. **Method:** A total of 415 cases of tumours of uterine cervix (ectocervix and endocervix) were studied.The clinical data was obtained from patients admitted in our hospital in Department of Gynaecology and Obstetrics.The specimens were received in different forms such as punch biopsy (381), hysterectomy (5) and polypectomy(29). These were fixed in 10% buffered formalin and were routinely processed with paraffin embedding and 3 to 5µ H and E sections were studied in all cases. **Results:**The majority of patients were in the age group of 41-46 years, (54.2%). Malignant tumours comprised of 367 cases (88.5%) of which majority presented in stage III disease and benign tumours comprised of 48 (11.5%) cases. The most common complaint in cases diagnosed with malignant and benign tumourswas bleeding per vaginum 135 cases (36.78%) and 23 cases (41.6%) respectively. The most common malignant tumour was keratinizing-squamous cell carcinoma (273; 81.77%) and benign tumour was endocervical polyp (31; 7.4%). **Conclusion:**The morphological diagnosis of uterine cervical tumours can be extremely difficult given the multitude of histopathological variants. One of the most important prognostic factors was the clinical staging of cervical tumors. Cervical biopsy is a cost effective investigation with a great bearing on the ultimate treatment and prognosis of patient.
Keywords: Cervical, Tumour, Specimens, Biopsy, Hysterectomy, Polypectomy, Formalin, Paraffin, Malignant, Benign.

Introduction
Cervical cancer was the most common malignancy in both incidence and mortality among women prior to the 20th century. Today, a dichotomy exists between developing and developed nations; the incidence of cervical cancer in the latter has fallen dramatically while the disease continues to be the second most common cancer in women worldwide [1]. At the same time cervical cancer is on the declining trend in India according to the population-based registries; yet it

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continues to be a major public health problem for women. As per population based cancer registry, the incidence of cervical cancer in India varies from 16.3 to 30.6 per lakh. The highest is seen in Chennai and lowest in Delhi [2].
Globally, approximately 570 000 cases of cervical cancer and 311 000 deaths from the disease occurred in 2018. India and China together made up more than one-third of the global cervical cancer burden in 2018, with India contributing with 97,000 cases and 60,000 deaths, while China recorded over 106,000 cases and 48,000 deaths.However, India recorded the highest estimated number of cervical cancer deaths [3].The cervical carcinomas are comprised of predominantly histological type of squamous cell carcinomas (SCC) (70%) followed by adenocarcinomas (20-25%) and adenosquamous carcinomas (2-5%). Very rarely, cancer can arise in other types of cells in the cervix [4].

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Although cancer of the cervix is not completely preventable, its incidence and prevalence can be reduced if screening programs are successfully applied to the population. The widespread screening with Pap smear has reduced mortality [5]. Thehistopathological studies of the cervix along with clinical correlation is very important for early diagnosis in diseases of the cervix as they have advantage of being readily available, relatively cheap and technically easy. Hence, the present study was undertaken to assess the spectrum of tumour and tumour like lesions affecting cervix and to elucidate pattern of pathologic changes that are commonly responsible for cervical pathologies in our community and their association with clinical factors. It also aims to determine the prevalence of different cervical pathologies and histological types of cervical cancer.

Materials and Methods

This prospective and retrospective study was carried out in total 415 female patients hospitalized in the Tertiary Care Hospital, in the Department of Pathology over a period of five years from 2012-2017.All the lesions of uterine cervix involving ectocervix and endocervix were included. Various lesions arising in the uterus, vulva, vagina and parametrium and not involving the uterine cervix were excluded. A detailed clinical history was recorded with reference to age, nature and duration of symptoms along with menstrual history, significant past history and other complaints. Local, general and systemic examination and all relevant investigations included pap smear /ultrasonography /CT scan/MRI. The clinical data was obtained from patients admitted in our hospital in the department of Gynaecology and Obstetrics. The biopsies were performed after obtaining consent from the patients. The specimens included in the study were received in different forms such as punch biopsy, hysterectomy and polypectomy specimens. These were fixed in 10% buffered formalin and were routinely processed with paraffin embedding and 3 to 5μ H and E sections were studied in all cases. Special stains like mucicarmine, PAS etc were employed whenever necessary. The diagnosis was made on light microscopy.

Observations and Results

A total of 415 cases were studied during a period of five years.Age of the patients ranged from 21-80 years with mean age of 49.96 years. The maximum numbers of patients were in the age group of 41-60 years (54.2%) followed by 21-40 (27.5%) and 61-80 years (18.3%).Themost common single presenting complaint was bleeding per vaginum in 158 (38.1%) cases and other clinical presentations are shown in table 1. Among 367 cases diagnosed with malignant tumours 135 (36.78%) cases presented with bleeding per vaginum while among 48 cases diagnosed with benign tumours23 (41.6%)also presented with bleeding per vaginum.

Table 1: Distribution of patients according to clinical presentation

Symptoms	Frequency	Percentage
Bleeding PV (B)	158	38.1
Post-menopausal bleeding (PMB)	71	17.1
Dysfunctional uterine bleeding (DUB)	51	12.3
Bleeding PV, Pain (BP)	39	9.4
Pain in abdomen (P)	32	7.7
Foul smelling discharge (FS)	27	6.8
White discharge (W)	12	2.9
Post coital bleeding (PCB)	08	1.9
Foul smelling, pain	06	1.4
White discharge, pain	03	0.7
Bleeding PV, Foul smelling	02	0.5
Bleeding PV, PMB	01	0.2
Bleeding PV, DUB	01	0.2
Pain, DUB	01	0.2
PCB, pain	01	0.2

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PMB, white discharge	01	0.2
White discharge, foul smelling	415	100

Table 2 show the clinical findings of all the cases and most common finding was erosion observed in 48.19% cases.

Table 2: Clinical examination of patients

Clinical findings	Frequency	Percentage
Erosion	200	48.19
Polyp	34	8.19
Growth-bleeds on touch	43	10.3
Exophytic growth	91	21.92
Thickening of cervix	08	1.9
Barrel shaped cervix	03	0.7
Erosion, bleeds on touch	20	4.8
Bleeds on touch, thickening of cervix	06	1.4
Exophytic growth, erosion	02	0.4
Exophytic growth, thickening of cervix	02	0.4
Erosion, thickening of cervix	03	0.7
Exophytic growth, bleeds on touch	02	0.4
Total	415	100

The malignant tumours comprised of 367 cases (88.5%) and benign tumours comprised of 48 (11.5%) cases. Among the malignant neoplasms, majority of were para 3 (129; 35.14%) followed by para 4 (124; 33.78%), para 2 (89; 24.25%)and para 5 (20; 5.4%).

There was only one case of nulliparous woman. The clinical examination in benign and malignant tumours shows that erosion was the most common findings in both the tumours as shown in figure 1.
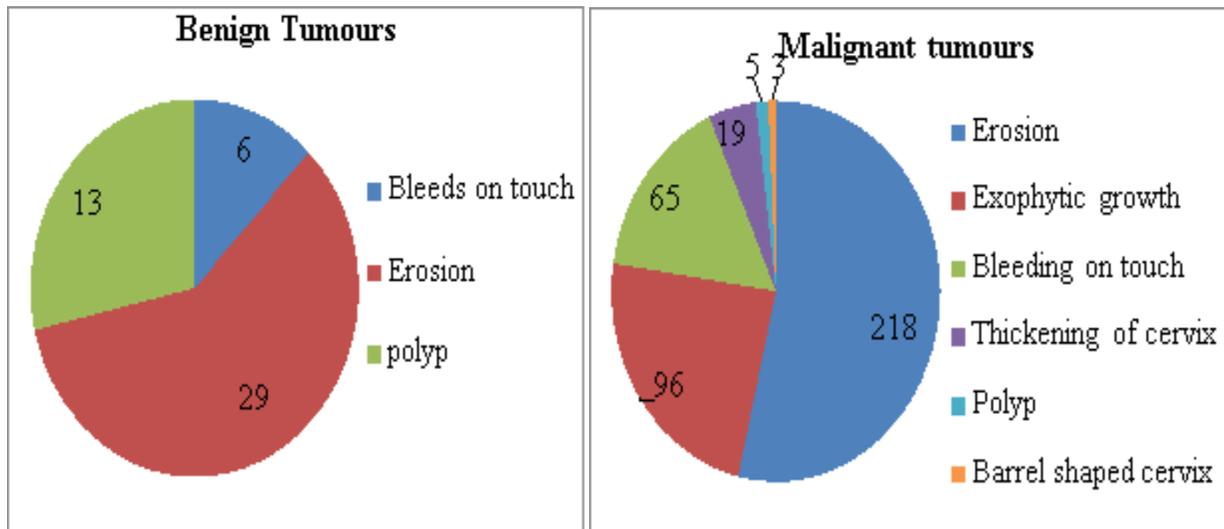
Fig. 1: Clinical examination in benign and malignant tumours

The majority of patients (165; 45%) presented with stage III disease, 91 cases (30%) presented with stage IV disease, 65; 15% with stage II and remaing 30; 10% presented with stage I disease.

Cervical biopsies comprised of 381 (91.8%) cases followed by polypectomy (29; 6.9%) and hysterectomy specimens (5; 1.2%) as depicted in figure 2.Out of 381 biopsies, 363 were malignant lesions and 18 were benign. Out of 29 cases who presented with a polypoidal growth; 21 cases were classified as endocervical polyp, 4 cases were fibroepithelial polyp, 3 were leiomyomas and one case was keratinizing squamous cell carcinoma. Out of 5 cases of hysterectomy, 4 were total Wertheim's hysterectomy specimens and 1 specimen was a simple hysterectomy specimen done for cervical leiomyoma.
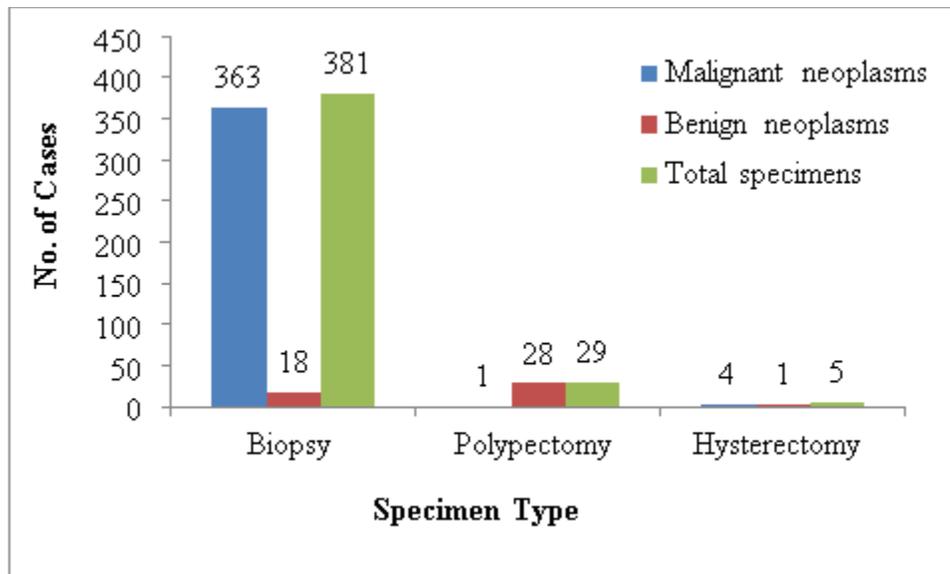

Fig. 2: Distributrion of malignant and benign neoplasm in different specimen type

Malignant squamous tumours were 334 (91.1%) cases and malignant glandular tumours were 19 (5.1%) which included endocervicaladenocarcinoma and endometroid adenocarcinoma. There were 14 (3.4%) cases of malignant tumours of other epithelial tumours.

The most common malignant tumour was keratinizing (K) - squamous cell carcinoma (SCC) (81.77%) and most common benign tumour was endocervical polyp (7.4%) as shown in table 3 and figure 3.

Table 3: Frequency of different histopathological types of benign and malignant tumours according to WHO Classification

Type of tumor	Histopathological type	No. of cases	Total
Squamous Malignant tumors	SCC-K	273 (81.77%)	334 (80.5%)
	SCC- NK	37 (11.07%)	
	CIN III	16 (4.79%)	
	Papillary	4 (1.19%)	
	Warty	2 (0.59%)	

	Lymphoepithelioma-like	2 (0.59%)	
Squamous Benign tumors	Fibroepithelial polyp	5 (1.20%)	5 (1.20%)
Glandular malignant tumors	Endocervical adenocarcinoma	11 (57.89%)	19 (4.6%)
	Endometroid adenocarcinoma	8 (42.11%)	
Glandular benign tumors	Endocervical polyp	31 (7.4%)	31 (7.4%)
Other epithelial malignant tumors	Adenosquamous carcinoma	8 (57.14%)	14 (3.4%)
	Glassy cell variant	6 (42.86%)	
Mesenchymal benign tumors	Leiomyoma	12 (2.9%)	12 (2.9%)
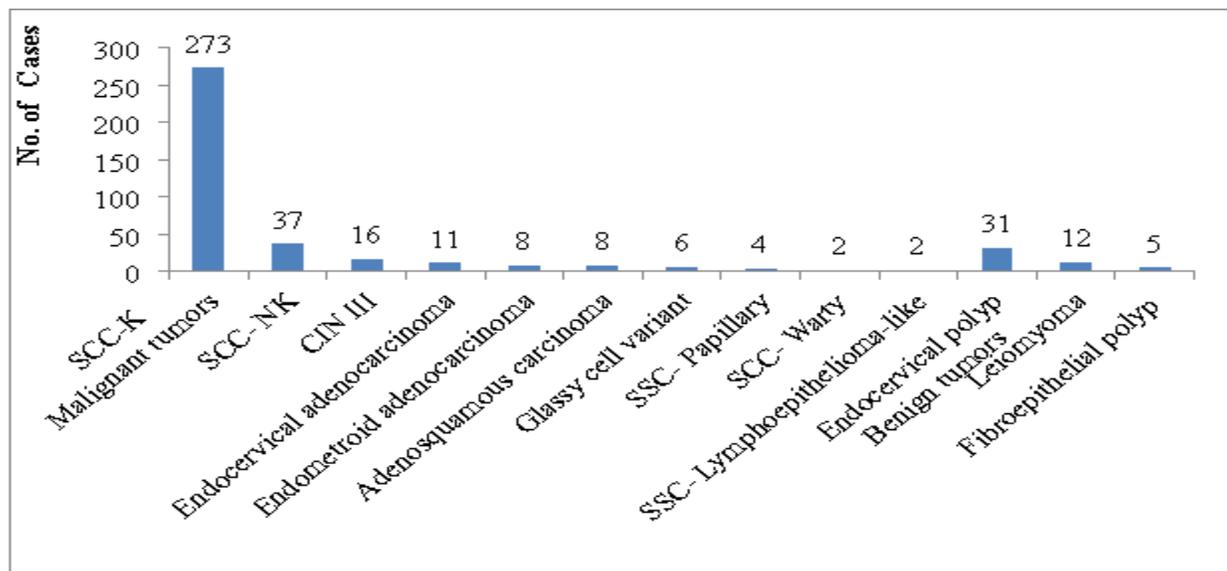
Fig. 3: Malignant and benign tumours of uterine cervix in decreasing order of frequency

Discussion

Cervical cancer continues to be a major public health problem affecting middle-aged women, particularly in less-resourced countries.It is estimated that about 160 million women between the ages of 30 and 59 years are at risk of developing cervical cancer in India, with 96,922 new cases registered in 2018 alone[1, 3].In the present study, mean age of patients with malignant neoplasms was 48.86 years which is similar to study done by Nigatu et al [6]. The mean age of patients with benign neoplasms was 40 years. The overall mean age of 415 patients was 49.96 years, these findings are similar to other researchers [7, 8]. The incidence of invasive carcinoma of cervix shows an increasing trend with increasing age with majority of patients presenting in their 5th and 6th decades of life. Total of 367 cases had malignant neoplasms, majority of them were para 3 (35.14%) followed by para 4 (33.78%), para 2 (24.25%) and para 5 (5.4%) while there was only one case of nulliparous woman. The parity of patients in malignant lesions is comparable with previous studies [9, 10]. Also, other studies corroborate the positive relationship between high parity and cervical cancer [11, 12]. The implications of early sexual intercourse, early pregnancy and parity which were observed in

earlier studies are similar to the finding of current study with emphasis on the increased frequency of malignant neoplasms of cervix in multiparous women. Parity has no implication in the incidence of benign neoplasms of the uterine cervix.

The majority of women with malignant tumours present with bleeding per vaginum on douching and coitus with associated pain in more than half the patients. Other significant complaints included abnormal bleeding in perimenopausal women and white discharge with or without foul odour. Although postcoital bleeding can occur in a variety of benign causes; it is considered as the cardinal symptom of cervical cancer [13]. Most of the patients (76%) with malignant lesions, presented with an erosion followed with findings of exophytic growth in 20% of the cases. A minority of patients (2%) showed evidence of predominantly endophytictumor leading to thickened cervix with nodularity and barrel shaped cervix. Chitkara [14] reported that cervical malignancies presenting as erosion can be missed by the naked eye and hence coloposcopic examination and biopsy of all suspicious lesions is a must. Out of 48 benign cases, most common finding on per speculum examination was a polypoidal mass in 29 cases (60.4%), followed by erosion in 14 cases (29.16%).Majority of women presented in stage III followed by stage IV and II whereas in Western studies, majority of women presented in stage I. This late stage of presentation of women in existing study can be attributed to the variable clinical presentation of disease which women mistake to be of less significance and lack of knowledge and awareness regarding the symptoms of cervical neoplasms.

On histopathological examination, out of 381 biopsies, 363 turned out to be malignant and 18 were benign neoplasms. Out of 381 cervical biopsies, 16 cases of CIN III were diagnosed which was found to be 4.35% of the total malignant tumours of the cervix which is comparable with the study conducted by Nigatu et al [6]. Out of 5 hysterectomy specimens, 4 turned out to be malignant neoplasms and 1 was leiomyoma and out of 29 polypectomy specimens, 28 were benign neoplasms and only one case was of malignant neoplasm.

The tumours of uterine cervix were classified according to the WHO classification to study the pattern, distribution and frequency of benign and malignant neoplasms affecting the uterine cervix.The commonest histological type of cervical cancer was malignant squamous cellcarcinoma with a prevalence

of 91.1%which are in accordance with the previous studies [15-17]. 4.5% (19 cases) were malignant glandular neoplasms of which 11 cases (57.89% of total adenocarcinoma tumours) were of endocervical type of mucinous adenocarcinoma and the remaining 8 cases (42.1%) were endometrioid type of adenocarcinoma. Therefore in present study majority of the cases were of the mucinous endocervical type of adenocarcinoma. These findings are comparable with the study conducted by Barbu et al [18]. According to Kurmann et al [19] histopathologically, the two most common subtypes of cervical adenocarcinomas are the mucinous endocervical type and the endometrioid type. Total of 14 (3.4%) malignant adenosquamousneo plasms, out of which 8 were adenosquamous carcinomas and 6 were clear cell variant of adenosquamous carcinomas. These findings are correlated with many other studies wherein the incidence of adenosquamous neoplasms was found to be 3-5% [20, 21]. The importance of diagnosing the adenosquamous carcinoma is due to the poor prognosis associated with this variant of malignant cervical epithelial tumours.

Out of total 48 benign neoplasms, 36 were benign epithelial polyps, which included endocervical and fibroepithelial and 5 were leiomyomas. This study showed 8.6% cases tobe benign cervical polyps (endocervical and fibroepithelial). This finding is similar to the study done by Asgharet al [22]. We diagnosed 12 cases of cervical leiomyomas, which accounted to 2.8% of the total neoplasms of the uterine cervix. Cervical leiomyomas are uncommon neoplasms that develop in the wall of cervix. The primary treatment modality includes myomectomy or hysterectomy in cases of large tumours which are symptomatic.

Conclusion

The present study revealed that morphological diagnosis of uterine cervical tumours can be extremely difficult given the multitude of histopathological variants, each with different possible biological behavior. It is important to differentiate and diagnose benign neoplasms, because of its close clinical mimic to malignant neoplasms. The clinical staging of tumours of the uterine cervix has been considered as one of the most important prognostic factor. The high proportion of invasive carcinoma and late presentation of the patients indicates the need to investigate delay factors and implement early diagnosis and cost effective treatment programs. Initiation of effective cervical screening programs is mandatory to prevent

mortalities and morbidities associated with the cervical cancer. Cervical biopsy is a cost effective investigation with a great bearing on the ultimate treatment and prognosis of the patient.

References

1. Sreedevi A, Javed R, Dinesh A. Epidemiology of cervical cancer with special focus on India. Int J Womens Health. 2015;7:405–414.
2. Arulponni TR, Janaki MG, Nirmala S, Ramesh B S , Rishi K S , Kirthi K. Carcinoma cervix treated with Radiotherapy – our experience with emphasis on our concerns. J ObstetGynecol India 2010;60(1) : 61-65.
3. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, Bray F. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health 2020;8: e191–203.
4. Spaans VM, Trietsch MD, Peters AA, et al. Precise Classification of Cervical Carcinomas Combined with Somatic Mutation Profiling Contributes to Predicting Disease Outcome. PLoS One. 2015;10(7):e0133670.
5. SafaeianM, Solomon D, Castle PE. Cervical cancer prevention--cervical screening: science in evolution. ObstetGynecolClin North Am. 2007;34(4):739-ix.
6. Nigatu B, Gebrehiwot Y, Kiros K, Eregete W. A five year analysis of histopathological results of cervical biopsies examined in a pathology department of a teaching hospital (2003-2007). Ethiopian journal of reproductive health 2010;4:1.
7. Shetty T, Kairanna N., Singh B.M.K., Pavithra P., Singh V.K. The spectrum of neoplasms of uterine cervix and their clinico-morphological correlation in tertiary care center in dakshina Karnataka. Trop J Path Micro 2018;4(7):486-490.
8. Krishnappa C, Kanabur DR, Dinesh CU. Clinico-morphological Spectrum of Neoplasms of Uterine Cervix in a Tertiary Care Center in North Karnataka, South India. Int J Sci Stud 2016;4(2):6-12.
9. Shaki O, Chakrabarty BK, Nagaraja N. A study on cervical cancer screening in asymptomatic women using Papanicolaou smear in a tertiary care hospital in an urban area of Mumbai, India. J Family Med Prim Care. 2018;7(4):652-657.
10. Agarwal S, Vishnoi R, Gandagule VN, Chauhan SS, Carcinoma of the uterine cervix. Ind J Cancer 1968;123-126.
11. Brinton LA, Reeves WC, Brenes MM, et al. Parity as a risk factor for cervical cancer. American Journal of Epidemiology 1989; 130:486–496.
12. Thomas DB, Qin Q, Kuypers J, et al. Human papillomavirus and cervical cancer in Bangkok. II. Risk factors for in situ and invasive squamous cell cervical carcinomas. American Journal of Epidemiology 2001; 153:732–739.
13. Tarney CM and Han J. Postcoitalbleeding: a review on etiology, diagnosis, and management. Obstetrics and Gynecology International 2014; Article ID 192087: 1-8.
14. Chitkara NL. Cancer in Punjab. Ind J Cancer 1965;3:94-105.
15. Preeti, Kalhan S, Alka, Jain K, Arora KS. Should mucinhistochemistry be routinely done for carcinoma cervix. Journal of Clinical and Diagnostic Research 2010; 4(4):2714-2719.
16. KrennHrubec K, Mrad K, Sriha B, Ayed F B, Boltalico DM, Ostolaza J et al. HPV Types and Variants Among Cervical Cancer Tumours in Three Regions of Tunisia. J Med Virol. 2011; 83(4): 651-57.
17. Irabor GI, Omotoso AJ, Isiwele EM, Nnoli AM, Omoruyi KA. Histopathological study of cervical cancer specimen at the university of calabar teaching hospital, calabar. Med. Res. Chron. 2017;4(5):582-590.
18. Barbu L, Craitoiu S, Margaritescu CL. Cervical adenocarcinoma: a retrospective clinicopathologic study of 16 cases. Rom J of MorpholEmbrol 2012;53:615-624.
19. Kurmann RJ, Norris HJ, Wilkinson E. Tumors of the cervix, vagina and vulva, Atlas of tumor pathology, 3rd series (fascicle 4), Armed forces institute of pathology, Washington DC 1992;83-95.
20. Lea JS, Coleman RL, Garner EO, Duska LR, Miller DS, Schorge JO. Adenosquamous histology predicts poor outcome in low-risk stage IB 1 cervical adenocarcinoma. GynecolOncol 2003;91:558-62.
21. dos Reis R, Frumovitz M, Milam MR, Capp E, Sun CC, Coleman RL, Ramirez PT. Adenosquamous carcinoma versus adenocarcinoma in early-stage cervical cancer patients undergoing radical hysterectomy: An outcomes analysis. GynecolOncol. 2007 Dec;107 (3):458-63.
22. Asghar S, Afzal H, Shaukat A, Ayub R. The frequency of pathology in women presenting with postcoital bleeding: Lahore J 2008;3 :14-20.

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