

## The pattern of occurrence of female genital tract malignancies at a tertiary care centre in Northern India in last ten years

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### Abstract

To analyze the pattern of occurrence of female genital tract (FGT) cancers at a tertiary care centre in Northern India in last one decade (2007-2016). In this retrospective study, data was collected for the past 10 years from department of radiotherapy KGMU, Lucknow and analyzed with SPSS software. A total of 30,705 patients with malignancy were registered, 13,482 (43.91%) were females, of which 5717 (18.62%) were diagnosed with female genital tract cancers. The trend shows that the number of patients presenting with FGT cancers had been doubled in 2016 comparison to that in 2007, though the proportion of FGT cancers out of patients presenting with any malignancy remain similar. Cancer cervix is the major bulk followed by cancer ovary and cancer endometrium. Cancer vulva and vagina are less common but their number is also increasing every year. On average, FGT cancers represent one fifth of all malignancies and one half of all malignancies in females with no significant rise in presentation throughout last ten years. Increasing awareness for FGT malignancies is the need of hour.

**Keywords:** Female genital tract (FGT) cancers, Northern India

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### Introduction

In past few decades, better education has led to better job and income leading to more sedentary lifestyle, more consumption of high calorie food, alcohol and smoking. These factors along with increased life expectancy has put large burden of non communicable chronic diseases like diabetes, hypertension and cancers.<sup>(1)</sup>

During the last 20 years, India has emerged as a fast growing economy with changes in lifestyle-related behaviour partially responsible for the increasing cancer burden; cancer is among top three killers among adults in both rural and urban India.<sup>(1)</sup> Few decades ago, cancer was 6<sup>th</sup> leading cause of death in industrialised countries, today it is the second leading cause of death.<sup>(2)</sup> As low human developmental index(HDI) countries become more developed and more "westernized", disease pattern is also showing a "western effect". The westernization effect is a reduction in infection related cancers and increase in cancers associated with reproductive, dietary and hormonal risk factors.<sup>(2)</sup>

In India in 2012, 10.15 lac new cancer cases occurred. Of these 4.77 lac were males and 5.37 lac were females, overall incidence is 92.4 per lac population and mortality rate was 69.7 per lac population.<sup>(2)</sup>

The first registry in India was established in Mumbai in 1963 and a major expansion took place from 1982 with the formation of the National Cancer Registry Programme.<sup>(1)</sup> The Indian Council of Medical

Research initiated a network of cancer registries under the National Cancer Registry Programme (NCRP) in 1981 and data collection commenced in these registries from January 1982.<sup>(1)</sup> However, India being a vast country, setting up of new registries throughout the country involves enormous cost in establishing and maintaining the same. Therefore 'Development of an Atlas of Cancer in India' with a cost-effective design and plan using advances in modern electronic information technology was conceived, to collect and process relevant data on cancer. This Atlas gave an overview of patterns of cancer in different parts of India besides calculating estimates of cancer incidence, wherever feasible.<sup>(3)</sup> In present study, we have analyzed last 10 years data from KGMU, Lucknow, (tertiary care centre) to find types and age group of peak incidence of FGT in this part of globe.

### Materials and Method

In this retrospective study, data of all cancer patients registered at the Department of Radiotherapy, King George's Medical University, Lucknow (A tertiary care centre) for 10 years i.e. 2007-2016 has been included and analyzed with SPSS software version 16 to find out number, proportion of different FGT cancers and age group of peak occurrence.

### Results

Total no of cancer patients presenting to Department of Radiotherapy (both Indoor & Outdoor), King Georges Medical University, Lucknow (tertiary

care centre) for 10 years i.e. 2007-2016 is 30,705. The number of total cancer patients, female patients of all types cancers and of female genital tract cancers are increasing year by year. (Table 1) Out of total 30,705 patients of cancer, female patients were 13,482 (43.91%). Total no. of cases of female genital tract cancers, in the same duration, is 5,717 (18.62%), though the proportion contributed by FGT cancers to the total cancers remains similar (around one fifth).

Amongst cancers of female genital tract major bulk is Cancer Cervix accounting 86.05% of total female

genital tract cancers followed by Cancer Ovary(6.32%), Cancer Endometrium(4.0%).(Table 2)

Cancers of Vulva and Vagina contribute small proportions to the total female genital tract cancers i.e. 0.93% and 0.44% respectively. Vault cancers are actually the cases of ca cervix and endometrium which are incompletely cured surgery, got recurrences and present with complaints of vaginal bleeding (growth and ulcers) etc. and such cases contribute to 2.23% of total female genital tract cancers. In present study, 87.4% of all FGT cancers are HPV associated cancers.

**Table 1: Total and female genital tract (FGT) cancer patients and percentage**

Year	Total patients	Total females	%	FGT cancer patients	%
2007	1347	624	46.32	304	48.72
2008	2593	1147	44.23	536	46.73
2009	2748	1288	46.87	566	43.94
2010	2872	1248	43.45	570	45.67
2011	3094	1417	45.81	665	46.93
2012	3408	1563	45.86	677	43.31
2013	3705	1592	42.97	540	33.91
2014	3712	1571	42.32	650	41.37
2015	3625	1505	41.52	588	39.06
2016	3601	1527	42.40	621	40.66
Total	30,705	13,482	43.91	5717	42.41

**Table 2: Year wise distribution of all female genital tract cancers (with percentage)**

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Cervix (%)	264 (86.8)	479 (89.4)	489 (86.4)	502 (88.1)	589 (88.6)	594 (87.7)	459 (85.0)	540 (83.1)	485 (82.5)	519 (83.9)
Ovary (%)	26 (8.6)	29 (5.6)	38 (6.7)	25 (4.4)	29 (4.4)	33 (4.9)	42 (7.8)	54 (8.3)	44 (7.5)	40 (6.4)
Endometrium(%)	8 (2.7)	20 (3.9)	25 (4.4)	27 (4.7)	25 (3.7)	28 (4.1)	17 (3.1)	14 (2.2)	31 (5.2)	34 (5.4)
Vulva (%)	5 (1.6)	2 (0.4)	1 (0.3)	2 (0.4)	3 (0.5)	5 (0.7)	9 (1.7)	6 (0.9)	11 (1.9)	9 (1.4)
Vagina (%)	1 (0.3)	2 (0.4)	1 (0.2)	1 (0.2)	4 (0.6)	2 (0.4)	3 (0.6)	3 (0.5)	3 (0.5)	5 (0.8)
Vault (%)	0 (0)	4 (0.7)	11 (1.9)	13 (2.2)	15 (2.2)	15 (2.1)	10 (1.9)	33 (5.0)	14 (2.4)	13 (2.1)
Fallopian Tube(%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.02)
v. mole(%)	0 (0)	0 (0)	1 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	304 (100)	536 (100)	566 (100)	570 (100)	665 (100)	677 (100)	540 (100)	650 (100)	588 (100)	621 (100)

**Table 3: Age group wise distribution of cancer cervix patients(%) in each study year**

ca cervix	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
≤ 30 yrs	4.2	3.7	3.9	4.7	3.0	4.3	4.1	3.1	2.0	2.6
31-40yrs	23.1	26.9	23.5	24.7	25.7	20.9	17.4	21.8	22.0	20.8
41-50yrs	36.7	33.1	35.7	30.8	32.8	35.0	31.8	34.0	34.0	28.3
51-60yrs	24.2	24.1	26.7	22.9	24.4	25.9	37.0	27.7	26.6	34.1
61-70yrs	9.4	10.2	8.5	14.7	11.7	12.1	7.8	11.6	12.3	11.7
71-80yrs	2.2	1.9	1.1	1.7	2.0	1.5	1.5	1.2	2.4	1.9

≥ 81yrs	0	0	0.4	0.1	0.3	0.1	0.2	0.1	0.4	0.3
Total	100	100	100	100	100	100	100	100	100	100

**Table 4: Age group wise distribution of endometrial cancer patients (%) in each study year**

Cancer endometrium	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
≤ 30 yrs	0	0	3.8	0	0	0	0	0	0	2.9
31-40yrs	12.5	5	7.6	3.7	8.0	10.7	11.7	21.4	19.3	14.7
41-50yrs	37.5	30	23.0	22.2	36	28.5	11.7	28.6	19.3	26.4
51-60yrs	25	40	38.4	44.4	44	35.7	47.0	28.6	35.4	32.3
61-70yrs	25	25	23.0	29.6	8.0	21.4	17.6	21.4	25.8	17.6
71-80yrs	0	0	3.8	0	4.0	3.6	11.7	0	0	5.8
Total	100	100	100	100	100	100	100	100	100	100

**Table 5: Age wise distribution of ovarian cancer patients (%) in each study year**

ca ovary	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
≤30 yrs	19.2	24.1	15.7	20	6.8	15.1	2.3	9.2	15.9	17.5
31-40yrs	23.0	19.2	18.4	20	6.8	42.4	16.6	20.3	25	30
41-50 yrs	26.9	31.0	31.5	20	31.0	21.2	30.9	37.0	38.6	30
51-60 yrs	26.9	24.1	18.4	28	34.4	15.1	35.7	34.2	13.6	10
61-70 yrs	3.8	3.4	14.2	8	20.6	6.0	9.5	1.8	6.8	10
71-80 yrs	0	0	7.1	4	0	0	4.7	0	0	2.5
Total	100	100	100	100	100	100	100	100	100	100

Most common age group for cancer cervix and cancer ovary is 41-50 years while for cancer endometrium, cancer vulva, cancer vagina and cancer vault is 51-60 years.

Mean age for cancer cervix was 49.53 yrs, for endometrial cancer was 53.76 yrs and for ovarian cancer was 45.57 yrs. Mean age for vaginal, vulvar and vault cancer was 52.16, 52.23 and 50.86 yrs respectively.

Single case of Choriocarcinoma (age -45 years) was reported in 2009 but this is not true incidence as cases of invasive Hydatiform mole and Choriocarcinoma are also medically and surgically managed by Department of Obstetrics and Gynaecology.

Single case of fallopian tube carcinoma (age-59 years) was reported in 2016. The patient was a case of primary fallopian tube cancer partially treated at some other institute.

**Discussion**

Female genital tract cancers contribute to a significant proportion of total cancer patients in India with cancer cervix being second most common cancer next only to ca breast in females.<sup>(2)</sup>

Cancers of cervix, vulva, vagina are mainly caused by epitheliotropic virus i.e. HPV<sup>(4)</sup> while cancers of endometrium, ovary and fallopian tube are caused by hormonal and genetic factors.<sup>(5)</sup> In present study female genital tract cancers are contributing 18.62% of total cancers.

Worldwide incidence and age standardised rate of cancer cervix is 7.9% and 14.0 respectively. While

same figures for India is 22.9% and 22.0.<sup>(2)</sup> Cervical cancer is the commonest cancer cause of death among women in developing countries.<sup>(6)</sup> Cancer cervix is the leading cause of morbidity and mortality in females in our country.

As per Awasthy S (2015) every year in India, 1,22,844 women are diagnosed with cervical cancer and 67,477 die from the disease. It is the second most common cancer in women aged 15–44 years.<sup>(6)</sup> Same study concluded that the peak age of occurrence of cervical cancer in India is between 55 and 59 years, and the highest age-adjusted rates are in Aizawl in the north eastern part of India at 24.3 per 100,000 women and most common age group for ca cervix is 51-60 yrs.<sup>(6)</sup>

However, in the present study we found that the most common age group for cancer cervix was 41-50 yrs (mean age = 49.53 yrs). The difference observed is probably due to the fact that most of the patients presenting at the institute belong to rural areas and such patients have higher chances of HPV infection due to less awareness, poor personal hygiene and negligible coverage of HPV vaccines. More permissive sexual behaviour and early age at first coitus and first child birth may also contribute to early presentation of cancer cervix than general population.

Mortality due to cervical cancer is also an indicator of health inequities as 86% of all deaths due to cervical cancer are in developing, low- and middle -income countries.<sup>(6)</sup> Rajendra A. Badwe et al (2014) reported that rate of cervical cancer are uniformly decreasing in all urban and rural registries.<sup>(1)</sup> While cervical cancer is declining in urban settings, it is still the leading cancer site among women across India.<sup>(1)</sup>

The decline rates for cervical cancer may be partly explained by greater awareness for genital hygiene, and visiting clinicians at pre-clinical stage,<sup>(1)</sup> preventive use of HPV vaccines in past decade might also have contributed a little. But in present study, number of patients of cancer cervix is increasing every year. The difference might be due to more number of patients reporting to tertiary care centre for registration, treatment and early pickup of such cases with application of various screening procedures on larger number of patients as a routine in health care set-ups (even at community and primary health centres).

Ovarian cancer has emerged as one of the common malignancies affecting women in India.

It is the sixth most common cancer and the seventh leading cause of cancer deaths among women worldwide.<sup>(7)</sup> Incidence and age standardised rate for cancer ovary worldwide is 3.65 and 6.1, and for India is 5.0% and 4.9 respectively.<sup>(2)</sup> It constitutes about 15-20% of all genital malignancies.<sup>(7)</sup> Ovarian cancer is more common in age group 40-60 yrs, has high risk factors such as presence of familial cancer like breast, endometrial etc., presence of BRCA 1 & 2 mutation, nulliparity, early menarche - late menopause and nulliparity.<sup>(8)</sup>

The Age Specific Incidence Rate (ASIR) for ovarian cancer revealed that the disease increases from 35 years of age and reaches a peak between the ages 55-64.<sup>(9)</sup> Most common age group in present study is 41-50 yrs with mean age 45.57 yrs.

P Basu did a study (2009) about patterns of care in ovarian cancer patients and concluded that ovarian cancer has the worst prognosis among all gynaecological malignancies. The overall 5-year survival is approximately 45%, primarily due to the late stage at first diagnosis of the disease.<sup>(7)</sup> Many of the patients receive suboptimal management due to logistics and socioeconomic constraints.<sup>(7)</sup> The median disease-free survival was only five months. The modifiable factors that can improve the survival from advanced ovarian cancer are the bulk of disease left behind after primary surgery and the compliance of patients to chemotherapy.<sup>(7)</sup>

Incidence and age standardised rate of cancer endometrium for world is 4.8% and 8.3, for India it is 2.3% and 2.3 respectively.<sup>(2)</sup> In US, 1 in 40 women develops endometrial cancer in her lifetime.<sup>(10)</sup> The incidence is higher in white population of US and lowest in India and Japan.<sup>(10,11)</sup> In India endometrial cancer ranks 3<sup>rd</sup> amongst genital malignancies next to cervix and ovary.<sup>(10)</sup> In our study also we have found the similar results. In current study, the most common age group for ca endometrium is 51-60 yrs with mean age 53.76 yrs, though the same has been reported as 55-64 years with mean age 61.0 years.<sup>(11)</sup>

In some parts of the world endometrial cancer accounts for 4-8% of all cancers, fourth position after breast, colon and lung cancers and approximately 7400

die from endometrial cancer.<sup>(8)</sup> However, in south east Asia, endometrial cancer is less common and lowest rates are from India.<sup>(10,12)</sup> Balasubramaniam G and others (2013) found that endometrial cancer is common in western women, and the rates are very high; however in India, the rates are as low as 4.3 per 100,000.<sup>(13)</sup>

Epidemiological studies indicate that estrogens, endogenous and exogenous, have a major role in endometrial cancer.<sup>(10)</sup> Increased or prolonged estrogen exposure, either because of early menarche or late menopause, obesity, nulliparity, anovulation, estrogen producing neoplasms or unopposed exogenous estrogen including tamoxifen therapy place a woman at increased risk of Endometrial Cancer.<sup>(12)</sup>

Hormone replacement therapy (HRT) with estrogen is associated with an eightfold increased incidence but the addition of progestin decreases this risk dramatically.<sup>(12)</sup> Radiation, hypertension and diabetes are also predisposing factors for endometrial cancer.<sup>(12)</sup> Low parity, lactation, use of combined oral contraceptives (COC), a diet low in fat and high in plant foods, and physical activity decrease the risk, OCP use for 5 years or more reduces the risk by 50%.<sup>(12)</sup>

Overall morbidity and mortality of Endometrial cancer is low because most patients present at early stage as abnormal bleeding per vaginum.<sup>(12)</sup> Mortality is higher in patients with age above 50 years of age, non-residents and illiterates.<sup>(13)</sup> The five-year rates indicated better prognosis for those aged less than 50 years, non-tobacco-chewers, with no family history of cancer, with localized disease and those treated with surgery either alone or as a combination treatment.<sup>(13)</sup> Overall 5 year survival in endometrial cancer patients is 92% as reported by G. Balasubramaniam and others.<sup>(13)</sup>

Vaginal and vulvar cancers do not account for a large proportion of gynaecologic malignancies but their impact is significant.<sup>(14)</sup> Vulvar cancers accounts for less than 1% of all cancers and 7% of all gynaecological cancers.<sup>(15)</sup> Most vulvar cancers occur after menopause with peak incidence between age 65-75 yrs.<sup>(15)</sup>

Due to a change in sexual behaviour and an increased rate of HPV infection among younger women, increased incidence of both diseases has to be expected.<sup>(16)</sup> Both are commonly seen in postmenopausal females, associated with infection with HPV,<sup>(15,16)</sup> lesions have precursors and display levels of dysplasia before progression to invasive disease,<sup>(14,16,18)</sup> more common in whites and may occur as multicentric neoplasia with history of ca cervix etc.<sup>(17)</sup> Both are mostly squamous cell carcinoma on histology.<sup>(15,17)</sup>

C. Dittmer and others (2011) have reported that the statistic incidence of vulvar carcinoma has been calculated between 2 and 7 cases per 100,000 women, carcinoma and mean age 72 years.<sup>(16)</sup> In present study most common age group for vulvar cancer is 51-60

years with mean age 52.23 years. Condition like Lichen sclerosis is a premalignant (4-7%) for ca vulva.<sup>(17)</sup>

Vaginal cancer accounts for 1-2 % of all gynaecological cancers, occurs mostly in sixth decade of life.<sup>(18)</sup> Incidence of vaginal carcinoma is 0.6–1.0 cases per 100,000 women and The mean age 74 years as reported by C. Dittmer and others.<sup>(16)</sup> Present study reports that most common age group for vaginal cancer is 51-60 years with mean age 52.16 years.

Vaginal cancer has many of the same risk factors as cervical cancer, including a strong association with persistent human papillomavirus infection. Descriptive studies of the epidemiology of vaginal cancer are scarce in the literature.<sup>(19)</sup> DES exposure in utero is associated with adenocarcinoma of vagina prolonged use of pessary, prior irradiation and immunosuppression is recognised as a risk factor.<sup>(19)</sup>

As reported by Wu X et.al, the incidence rates for all vaginal cancers combined were 0.18 per 100,000 female population for in situ cases and 0.69 for invasive cases. The median age of invasive cases was older than that of in situ cases. White women have increased rate as compared to Asian/ Pacific Islander (API).<sup>(19)</sup> Compared with the rate for white women, the age-adjusted incidence rate of invasive SCC was 72% higher ( $P < .05$ ) among black women, The rates for in situ SCC peaked at age 70 years and then declined, whereas the rates of invasive SCC increased continuously with advancing age.<sup>(19)</sup>

Incidence rates of vaginal SCC varied significantly by race, ethnicity, and age group. Black, API, and Hispanic women as well as older women had a high proportion of late-stage disease and a low 5-year survival rate.<sup>(19)</sup>

Primary carcinoma of fallopian tube is the rarest gynaecological malignancy less than 1%. Secondary carcinoma of fallopian tube is more common (90%) primary sites being ovary, uterus, breast and gastrointestinal tract.<sup>(20)</sup>

## Conclusion

Out of total 30,705 patients registered with cancer, 13,482 (43.91%) were females and FGT cancers accounted for 5717 cases (18.62%). Though the number of FGT cancers was increasing each year throughout the decade, but the proportion contributed by FGT cancers to the total cancers remain statistically similar. This increase in number of cases may also be partially explained by increased reporting of cases consequent to increased awareness, referrals and improved healthcare facilities.

Cancer cervix was the most common FGT cancer ( $n= 4920$ , 86.05%). It is the second most common cancer affecting women in India, next only to breast. Increasing number of patients are being identified with wider use of screening procedures and availability of such procedures at primary health centre levels.

In our study, major FGT cancers (i.e. cancer cervix, ovary and endometrium) are presenting at earlier age in this population as compared to other studies. This may be alarming and need further research to find out whether it is the effect of better screening/ healthcare facilities or because of some other nutritional, dietary, social or environmental factors.

87.4% of total FGT cancers are HPV associated cancers (cancer cervix, vulva & vagina). Awareness about screening techniques and pre-malignant conditions is required to decrease the burden of such cases in society. In fact, considering this large figure, HPV vaccine should be recommended as universal in India at adolescent age group and its role in prevention, long term effects and efficacy needs to be statistically analyzed for which long term larger trials are needed.

## References

1. Rajendra A. Badwe,\*, Rajesh Dikshit, M. Laversanne and Fredie Bray Cancer Incidence Trends in India. *Jpn. J. Clin. Oncol.* (2014) 44(5):401-407.
2. K.Park. Epidemiology of chronic and non communicable diseases In: Park's textbook of Preventive and Social Medicine, 23<sup>rd</sup> edition, Jabalpur, M/S Banarasisdas Bhanot, 2015,6:381-382.
3. A. Nandakumar, T. Ramnath & Meesha Chaturvedi The magnitude of cancer cervix in India Indian J Med Res 130, September 2009, pp 219-221.
4. Viens LJ, Henley SJ, Watson M, Markowitz LE, Thomas CC, Thompson TD et al. Human Papillomavirus-Associated Cancers - United States, 2008-2012. *MMWR Morb Mortal Wkly Rep.* 2016 Jul 8;65(26):661-6.
5. Jaime Prat. Pathology of cancers of the female genital tract. *Int J Gynaecol Obstet.* October 2015;131(2):132–145.
6. Aswathy Sreedevi, Reshma Javed, and Avani Dinesh Epidemiology of cervical cancer with special focus on India *Int J Womens Health.* 2015;7:405–414.
7. P Basu, P De, S Mandal, K Ray, J Biswas Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, eastern India. *Indian Journal of Cancer.* 2009,46(1):28-33.
8. Hiralal Konar, Genital Malignancy in DC Dutta's Textbook of Gynaecology, 8th edition, Kolkata. 2016,24: 304.
9. Murthy NS1, Shalini S, Suman G, Pruthvish S, Mathew A Changing trends in incidence of ovarian cancer - the Indian scenario. *Asian Pac J Cancer Prev.* 2009;10(6):1025-30.
10. Hiralal Konar, Genital Malignancy in DC Dutta's Textbook of Gynaecology, 8th edition, Kolkata.2016,24: 292.
11. Howlader, N., et al. SEER Cancer Statistics Review, 1975-2008. 2011 [cited 2011; based on November 2010 SEER data submission]. Available from: [http://seer.cancer.gov/csr/1975\\_2008/](http://seer.cancer.gov/csr/1975_2008/).
12. Chhabra s, Tembhare a, Current status of endometrial carcinoma *J Mgims,* September 2009,14,(ii),18–23.
13. Balasubramaniam G, Sushama S, Rasika B, Mahantshetty U. Hospital-based study of endometrial cancer survival in Mumbai, India. *Asian Pac J Cancer Prev.* 2013;14(2):977-80.
14. Buchanan TR, Graybill WS, Pierce JY. Morbidity and mortality of vulvar and vaginal cancers: Impact of 2-, 4-,

- and 9-valent HPV vaccines. *Hum Vaccin Immunother.* 2016 Jun 2;12(6):1352-6.
15. David M. Luesley, Dewhurt's textbook of obstetrics and gynaecology, 8<sup>th</sup> edition, London, John Willey and Sons Ltd, 2012,55:729.
  16. C. Dittmer, A. Katalinic, C. Mundhenk, M. Thill Epidemiology of vulvar and vaginal cancer in Germany July 2011, 284 (1),169–174.
  17. Hiralal Konar, Genital Malignancy In DC Dutta's Textbook of Gynaecology, 8th edition, Kolkata.2016,24:274, 278.
  18. David M. Luesley, Dewhurt's textbook of obstetrics and gynaecology, 8<sup>th</sup> edition, London, John Willey and Sons Ltd, 2012,55:740.
  19. Wu X, Matanoski G, Chen VW, Saraiya M, Coughlin SS, King JB, Tao XG. Descriptive epidemiology of vaginal cancer incidence and survival by race, ethnicity, and age in the United States. *Cancer.* 2008 Nov 15;113(10 Suppl):2873-82.
  20. Hiralal Konar, Genital Malignancy In DC Dutta's Textbook of Gynaecology, 8th edition, Kolkata. 2016,24:323.