Original Article

Obstetries & Gynaecology

Retrospective Study of Gynaecological Malignancies in Less than 35 Years of Age in Southern India

ANAGHA KAMATH, RADHA R. PAI

ABSTRACT

Aim of the Study: To study the incidence, diagnosis and the treatment aspects of genital malignancies in a group of young patients who were less than 35 years old.

Materials and Methods: This study was based on the surgical biopsy materials which were received in the histopathology laboratory of Kasturba Medical College, Manipal University, Mangalore, from 1st January 2006– 31st December 2010. The sources of the specimens were: in-patients biopsy and surgical specimens from the Lady Goshen Hospital and the Kasturba Medical College Hospital, Mangalore. The demographic data which included the age of the patients, the site of the tumour and the diagnosis, were extracted from the request forms and the patients' case files.

Results: The prevalence of cancer in the younger ages [<35yrs] was 14.2%. The mean age of the presentation was 28 years, (SD+5.12). Ovarian cancer was the most common (70.5%) cancer, followed by cervical cancer (16.3%), choriocarcinoma (7%) and endometrial cancer (2%). There is a rising incidence of cervical and endometrial carcinoma. Advanced stages pre-dominated (58.2%).

Conclusion: Targetting younger women for cancer screening and considering the possibility of malignancy in them is a necessity. This study also provided the basis for the further analysis of the female genital malignancies. The high incidence and the average early mean age of the presentation underlies the importance of the screening programmes and awareness campaigns in our community. Early diagnosis and treatment may help to preserve the fertility and to decrease the mortality. High risk screening could help to reduce the burden of the disease. Education would undoubtly prove to be the most effective challenging remedy.

Key Words: Genital malignancy, Ovary, Cervix

INTRODUCTION

More than 70,000 new cases of cervical uteri, 3-8% of ovarian and 0.5-4.8% of corpus uteri, 1-3% of vulvar and gestational trophoblastic tumours, and over 75,000 of breast cancers are reported in India every year [1]. The predictions of a possibility of an increased incidence of cervical malignancies in the younger women had been raised, way back in 1980 [2]. Ten cases of endometrial carcinoma in women who were <25 years were reported 3 decades ago [3]. According to the National Center for Health Statistics, cancer is the second leading cause of death in women who are 25-44 years of age. Furthermore, malignancies during pregnancy account for about 5% of all the maternal deaths [4]. Despite the relatively high frequency of occurrence of female genital tumours in India, there is still a paucity of awareness on this subject. Therefore, this study was aimed at observing the trend of gynaecological malignancies in the younger age group in our set up.

MATERIALS AND METHODS

This hospital based, retrospective study was based on the surgical biopsy materials which were received in the histopathology laboratory of Kasturba Medical College, Manipal University, Mangalore, from January 1st 2006–December 31st 2010. The sources of the specimens were: in-patients biopsy and surgical specimens from the Lady Goschen Hospital and Kasturba Medical College Hospital, Manipal. The demographic data which included the age of the patients, the site of the tumour and the diagnosis were extracted from the request forms and the patients' case files. The inclusion criteria were age:15-35yrs, sex:female and diagnosis: primary or secondary genital malignancy [ovary/uterus/cervix/fallopian tubes/vagina/vulva]. The results were analyzed by using the Chi-square test.

RESULTS

Among 604 cases of histologically confirmed genital cancers which were recorded during the 5 year period of the study with a mean annual total of 120 cases, 84 were in women of the 15–35 years age group . Thus, malignant tumours of the female genital tract in this age group accounted for 14% of all the gynaecological malignancies, with the mean age of presentation being 28 years (SD ± 5.12). In this study, ovarian cancer accounted for a majority (52%) of all the female genital cancers, followed by the cancer of the cervix (39.3%), choriocarcinoma (7%) and endometrial cancer [being the least common one (2%)] [Table/Fig-1).

[Table/Fig-3] demonstrates the yearly distribution of the gynaecological malignancies within the study period. There was a steep rise in the proportion of younger women from 9% (Jan 2006–Dec 2007) to 18% (Jan 2008–Dec 2010), which plateaued thereafter. [Table/Fig-4] depicts the parity distribution in our study.

A majority of the ovarian carcinomas (65%) presented in the age group of 26-35 years. [Table/Fig-2]. Surface epithelial tumours were the most common histopathological type, among which the youngest was a 15 yr old case of borderline mucinous tumour. Athough most of the cases (5/7) in the teenage group were germ cell tumours, 2 were borderline epithelial tumours. Cases of granulosa cell tumour [2], Krukenberg tumour following carcinoma of the breast [1] and poorly differentiated Sertoli-Leydig tumours [1]

Site	Number	%
Cervix	32	39
Ovary	44	52
Chorio carcinoma	6	7
Endometrial	2	2
Vulva	0	0
Vagina	0	0

[Table/Fig-1]: Site distribution of malignant tumours of female genital tract
χ^2=25-07 P=0.0029 Significant [chi-square].

Age	0vary	Cervix	Endometrium	Chorio
15-20	7 (16%)	0	0	1 (17%)
21-25	8 (19%)	1 (3%)	1 (50%)	3 (50%)
26-30	14 (32%)	8 (25%)	0	0
30-35	15 (33%)	23 (72)%	1 (50%)	2 (33%)
TOTAL	44 (100%)	32 (100%)	2 (100%)	6 (100%)

[Table/Fig-2]: Age and Site distribution of malignant tumours of female genital tract
χ^2=25.07 P=0.0029 Significant, [chi-square] Mean age 28.46 +/- 5.12 yr.

Year	Total	15–35	%
2010	159	25	15.7
2009	131	23	17.6
2008	77	14	18.2
2007	122	11	9
2006	115	11	9.6
total	604	84	13.9

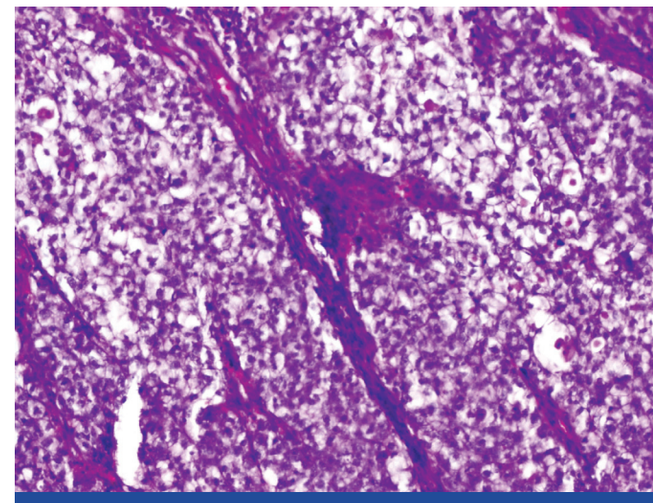
[Table/Fig-3]: Yearly distribution of malignant tumours of female genital tract
χ^2=4.401 p = 0.0359 (Significant <0.01 – chi square for trend).

	Ovary	Cervix	Endometrium	Chorio Carcinoma
Unmarried	7 (16)	0	0	0
Nulligravida	17 (39)	0	2	1 (17)
Nulliparous	0	0	0	3 (50)
Parous	5 (11)	6 (19)	0	2 (33)
Multiparous	15 (34)	26 (81)	0	0

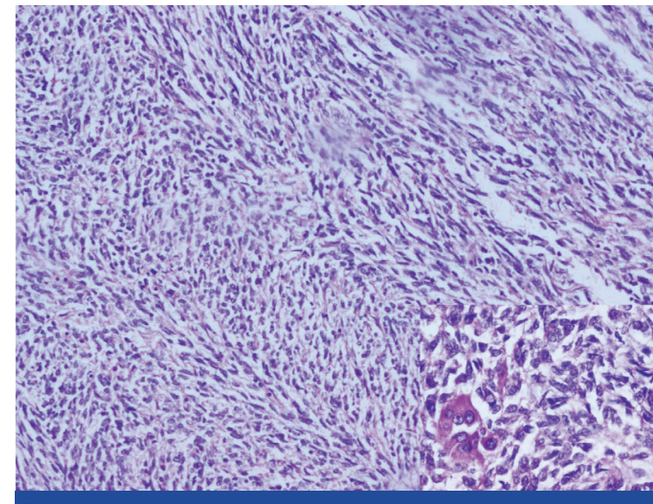
[Table/Fig-4]: Parity distribution in genital malignancy – ovary
χ^2=12 p<0.001 Vsig cervix χ^2 = 44.27 p<0.001 significant.

were also seen. Nearly 60% of the ovarian carcinoma cases were diagnosed at an advanced stage. Unilateral oophorectomy was done in 10 patients, among which in 6 patients, the diagnosis of malignancy was incidental and in 4, germ cell tumour was clinically suspected. Debulking was done in 6 patients, in 3 of these, following neoadjuvent chemotherapy. 6 patients in advanced stages were treated with chemotherapy.

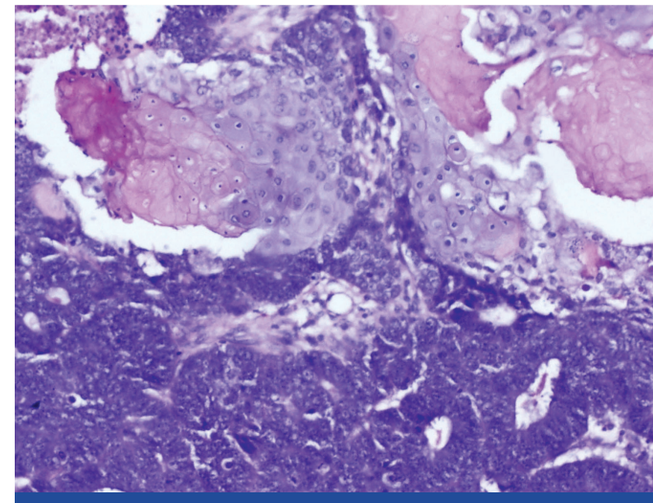
The peak incidence of cervical cancer was in the 30-35 years age group, while that of choriocarcinoma was in the 21-25 years age group. Squamous cell carcinoma was the pre-dominant type of cervical carcinoma. The youngest case in our study was a 22 year lady who was diagnosed at stage Ib1 [clear cell adenocarcinoma of cervix]. In all, 13(40%) cases were operable, while 2 patients were retroviral disease positive, with pulmonary tuberculosis. One case was detected coincidently during the medical termination of pregnancy. Wertheim's hysterectomy was done in 12 patients and 1 patient was discharged against medical advice. Neoadjuvant chemotherapy was given in 5 patients, out of which one developed a burst abdomen.



[Table/Fig-5]: Clear cell adenocarcinoma of cervix in a 22 year old woman

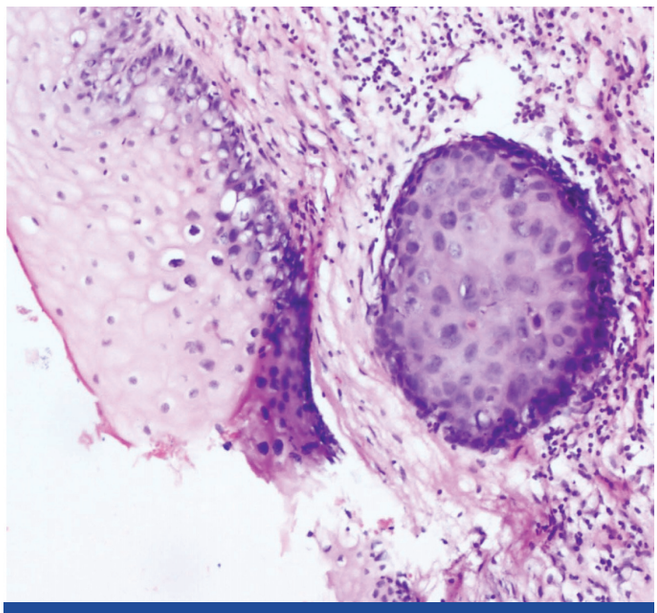


[Table/Fig-6]: Sertoli-Leydig cell tumour of ovary in a 19 year old lady



[Table/Fig-7]: Endometroid carcinoma with squamous metaplasia of ovary in a 33 year old woman

The youngest age of presentation of choriocarcinoma was a 19 yr old unmarried girl who presented with septicaemia. On emergency laparotomy, wide spread metastatic lesions were found to be present, her tissue biopsy revealed stage IV choriocarcinoma and the patient ended up with mortality. Three cases (50%) were preceded by molar pregnancies, 2 (33%) by term gestation and 1(17%) by abortion.



[Table/Fig-8]: Multifocal carcinoma in situ with micro invasion carcinoma cervix in a 25 year old woman

Endometrial carcinoma constituted 2% of the genital cancers (adenocarcinoma type). Both these patients had a history of infertility and were of the 30-35 year age group, with intractable menorrhagia.

DISCUSSION

The cancer which occurs between the ages of 15 and 30 years is 2.7 times more common than the cancer which occurs during the first 15 years of life, but it is much less common than the cancer in the older age groups, and it accounts for just 2% of all the invasive cancers [5]. It is noteworthy that cancer in the 15-29 years age group as a proportion of cancer at all ages is five times higher in India than England despite the actual incidence being lower in India [6]. This possibly reflects that a higher percentage (35%) of the women in India are in the age group of 15-35 years in the population pyramid [7].

The frequency distribution of the cancer types changes dramatically from the ages of 15-30 years, in such a way that the pattern at the youngest age does not resemble the one at the oldest age [5]. Malignant tumours of the female genital tract in the younger age group accounted for 14% of all the female cancers, while cancers of the ovary accounted for a majority of the cancers (52%), followed by cervical cancer (16.3%), choriocarcinoma (7%) and uterine carcinomas (2%). Although breast cancer is the most common tumour which affects women world wide, the cancer of the uterine cervix is still the most common one in the developing countries [8]. However, in the present study, although the prevalence of ovarian malignancy predominated the prevalence of all the female cancers, the prevalence of cervical cancer was very much comparable to that of ovarian carcinoma.

About 94% of the ovarian tumours are said to arise from the surface epithelium of the ovary [9]. Similarly, in this study, 70.5% of the ovarian tumours were of epithelial origin. The events which lead to malignant transformation within these cells are uncertain, but the risk factors that appear to be related to the development of the ovarian cancers include genetic, environmental and hormonal factors [10]. The vast majority of cases of cancer which are diagnosed before the age of 30, appear to be spontaneous and unrelated to either the carcinogens in the environment or family cancer syndromes. There are exceptions, but the exceptions are rare [5]. Therefore, the need to examine the ovaries as much as the need to visualise the cervix at every opportunity like the USG of the abdomen, sterlisation surgeries and caesarean sections is emphasized.

Fertility preserving conservative surgeries warrant an even greater importance in this age group. In the young women with stage Ia disease who are desirous of further childbearing, unilateral salpingo-oophorectomy may be associated with a minimal increased risk of recurrence, provided a careful staging procedure is performed and due consideration is given to the grade and the apparent self containment of the neoplasm [11].

The prevalence of the Krukenberg's tumours varies from 1% (incidental adnexal surgery) to 13% (surgery for pelvic masses) and up to 25% (autopsies or therapeutic oophorectomy) [12]. Bigorie V et al [13] and Ayhanet et al [14] reported respectively, 29 patients who were aged >16 years and 35 patients who were aged >22 years.

Within the UK, cervical cancer was the most common cancer in women who are less than 35 years of age ,with 702 cases being diagnosed in 2007 [15]. Between 2004–2008, the US incidence of cervical cancer in girls under the age of 20 was reported to be 0.1%, rising to 14.3% in women who were aged 20 to 24 years, of the total burden [16]. The probability of developing cervical cancer by age is: 1 in 638 for women who were aged 39 years and younger [17].

More than 70% of the women with cervical carcinoma were of the 30-35yrs age group, thus depicting the need for a prompt screening implementation in all the younger women. The high incidence frequency of carcinoma of the cervix could be attributed to early marriage and the high parity in our region. Epidemiological studies have consistently indicated that the risk of the cancer of the uterine cervix is strongly influenced by measures of sexual activity [18]. In India, HPV 16, 18, 31, 33 and 45 account for >92% of the squamous cell carcinomas and 95% of the cervical adenocarcinomas [19]. The well-known risk factors include a high number of live births, the long-term use (12 years or more) of oral contraceptives, tobacco smoking, lack of food which contains betacarotene, vitamins A, C and E and selenium [20,21]. The risk of cervical intraepithelial neoplasms (CINs) in HIV sero-positive women is at least 5 fold higher than in their sero-negative counterparts [18]. Implementing screening programmes has seen a major drawback in India as a result of illiteracy, the vast population and the lack of facilities at the peripheries.

Neoadjuvent chemotheraphy, followed by radical surgery, has proved to be valid alternative with a 48 % to 100% operability rate, with no influence on the surgery related morbidity. A pathologically confirmed compete response was detected in 9-18 % of the cases, the incidence of the lymph node metastasis being much lower than expected for the same stage and tumour size [22]. The complications of this combined modality include short term complications like (within 30 days from the end of the treatment) accidental injuries to the vessels, requirement of additional blood transfusion(s) (5%), bladder dysfunction (17%), lymphocysts (18%), abdominal wound dehiscence (2%) and ureteral stenosis/fistulas (1%). The long-term, severe complications are dyspareunia(10%), chronic neurologic bladder (7%) and vesico-ureteral, or recto-vaginal fistulas (3%) [23]. The tolerance of the combination therapy would probably depend on the age, diet and the body mass index.

A majority of the women in this study were averagely built and belonged to a low socio-economic strata.

Unlike other studies, in the present study, there was no significant difference in the parity of the ovarian carcinoma which was different from the usual prevalence, while the endometrial carcinomas were diagnosed in the nulligravida, but the maximum number of the patients with carcinoma of the cervix were multiparous. Contraception is protective against a majority of the genital tumours [24]. Unfortunately, the knowledge, awareness and the practice of this beneficial aspect is very low. Sterilisation was the only reported mode of contraception in our study.

Choriocarcinoma was found to be the second most common malignant tumour of the female genital tract in the African studies [25], but in this study, it accounted for only 7% of the tumours of the female genital tract. Considering that choriocarcinoma can complicate any conception and that its presentation may mislead clinicians, it is possible that the true frequency of this entity is very high than that which was suggested by this study. Throughout the world, the incidence rates for choriocarcinoma differ widely [26]. For example, in Europe and North America, choriocarcinomas are reported to affect one in every 30,000-40,000 pregnancies, and one in 40 molar pregnancies [27], whereas in Southeast Asia, rates as high as one in every 500-3000 pregnancies have been reported [28]. Although choriocarcinoma can be preceded by any gestational event, hydatidiform mole was found to be its most common precursor. The factors which were found to be associated with gestational trophoblastic neoplasia included professional occupation, a history of prior spontaneous abortions and the mean number of months from the last pregnancy to the index pregnancy [29]. Although persistent gestational trophoblastic disease has an excellent prognosis, non-compliance with the follow-up can lead to a delay in the diagnosis, and an inconsistent compliance with the treatment can lead to the development of chemotherapy-resistant disease. Factors such as access to contraception or timely health care, as well as genetic, dietary and other environmental influences, warrant further investigation [30].

The follow up was lost in our population, mainly due to ignorance and a poor socio-economic status. The regulations for the medical termination of pregnancy (MTP) may have been abused under the pretext of fertility regulation. Moreover, because of the lack of the MTP products for histopatholgical examination , the molar pregnancies could go undiagnosed. Inspite of the availability of standard investigative modalities in our government tertiary care centers at fairly reasonable rates, the below poverty line proportion hinders the efficiency today.

Radical management always triumphs over other reasonings due to a poor follow up. Criteria and issues such as risk adapted therapies to preserve the fertility, to reduce the adverse effects on the physical appearance and to avoid a surgical menopause, thereby receive negligible consideration in our centers unlike in the developed countries .

This data may not represent the accurate community prevalence rates . In India, the actual cancer statistics may be much more than that which is present in the hospital based data.

Management in the young is a real dilemma with tolerance and efficiency on one side and the problem of feminity, fertility, teratogenicity and the combination therapy of radiotherapy/neoadjuvant chemotherapy on the other side. The training modules should include a concern towards conservative surgeries like trachelectomy /cystectomy and also an approach to deal with cancer which complicates pregnancies. These findings could have a significant implication on the health planning and the clinical practice in our country. Furthermore, the emergence of new diseases such as the Acquired Immune Deficiency Syndrome may conceivably alter the pattern of the female genital malignancies [25].

CONCLUSION

Targeting younger women for cancer screening and considering the possibility of malignancy in them is a necessity. The need to examine the ovaries, as much as the need to visualise the cervix at every opportunity like USG of the abdomen and during procedures like laparoscopy, sterlisation and caesarean sections is emphasised. Endometrial evaluation is a must in patients with menorrhagia/infertility/polycystic ovarian syndrome at all levels of health care. An early diagnosis and treatment may help to preserve the fertility and to decrease the mortality. A high risk screening could help in reducing the burden of malignancy. Education would undoubtly prove to be the most effective challenging remedy. This study is a basis for the further analysis of the female genital malignancies in the young in India.

REFERENCES

[1] Devi KU. Current status of the gynaecological cancer care in India. *J Gynecol Oncol* 2009; 20:77–80.
[2] Beral V, Booth M. Predictions of cervical cancer incidence and mortality in England and Wales. *Lancet* 1986; 327:479- 95.
[3] Farhi DC, Nosanchuk J, Silverberg SG. Endometrial adenocarcinoma in women who are under 25 years of age. Obstet Gynecol 1986;68: 741-5.
[4] Rayburn WF .Foreword . Cancer Complicating Pregnancy .In, Leslie KK. Obstet Gynaecol Clin N Am. Philadelphia: Saunders 2005;13-4.
[5] Bleyer A, Vinyl A, Barr R, Introduction. In: Bleyer WA, O'Leary M, Barr R, Ries LAG (eds). Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000. National Cancer Institute, NIH Pub. No. 06–5767,2006;1-4.
[6] Arora RS, Alston RD, Eden TO, Moran A, Geraci M, O'Hara C et al. Cancer At Ages 15-29 Years ; The Contrasting Incidence In India And England. *Pediatr Blood Cancer* 2010 Oct 14 [Epub ahead of print].
[7] Park K. Demography and family planning. In: K. Park . Parks textbook of preventive and social medicine , 20th edition. Jabalpur, Banaridas Bhanot Publishers, 2009; 411.
[8] Olukoye AA. Cancers of the breast and cervix in Nigerian women and the role of primary health care. *Nig Med Practitioner* 1989;18:26-30.
[9] Monaghan JM. Malignant Disease of the Ovary. In: Edmonds DK . Dewhurst's Textbook of Obstetrics and Gynaecology for Postgraduate, 6th edition;Oxford: Blackwell Science Ltd, 1999;593.
[10] Nugent D, Salha O, Balen AH, Rutherford AJ .Ovarian neoplasia and subfertility treatments. *Br J Obstet Gynaecol* 1998;105:584-91.
[11] DiSaia PJ. The adnexal mass and early ovarian cancer . In , DiSaia and Creasman, *Clinical gynaecologic oncology*: 7th edition. Philadelphia, Elseviers, 2007;302-6.
[12] Garg R, Zahurak ML, Trimble EL, Armstrong DK, Bristow RE. Abdominal carcinomatosis in women with a history of breast cancer. *Gynecol Oncol* 2005;99:65-70.
[13] Bigorie V, Morice P, Duvillard P, Antoine M, Cortez A, Flejou JF et al Ovarian metastasis from breast cancer: report of 29 cases. *Cancer* 2010;116:799-04
[14] Ayhan A, Guvenal T, Salman MC, Ozyuncu O, Sakinci M,Basaran M et al. The role of cytoreductive surgery in non-genital cancers which were metastatic to the ovaries. *Gynecol Oncol.* 2005;98:235-41.
[15] Cervical cancer-UK incidence statistics. *Cancer research UK* 2006. http://info.cancerresearchuk.org/cancerstats/incidence/cervix.
[16] Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W et als (eds). *SEER Cancer Statistics Review*, 1975-2008, National Cancer Institute. Bethesda, MD, Available from URL: http://seer.cancer.gov/csr/1975_2008/,
[17] American Cancer Society-Cancer Facts &Figures2008.At:http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf (Accessed May 21, 2008).

[18] Spitzer M. Lower genital tract intraepithelial neoplasia in HIV infected women: Guidelines for evaluation and management. *Obstet Gynecol Surv* 1999 ;54:131-7.
[19] Paavonen J, Naud P, Salmeron J, Wheeler CM, Chow SN, Apter D et al. Efficacy of the human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infections and pre-cancer which are caused by the oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet* 2009;25:301-14.
[20] Kjellberg L, Hallmans G, Åhren AM, Johansson R, Bergman F, Wadell G et al . Smoking, diet, pregnancy and oral contraceptive use as the risk factors for cervical intra-epithelial neoplasia with respect to the human papillomavirus infection. *Br J Cancer* 2000;82:1332–8.
[21] Labani L, Andallu B, Meera M, Asthana S, Satyanarayana L. The food consumption pattern in the cervical carcinoma patients and the controls. *Indian J Med Paediatr Oncol* 2009;30:71-5.
[22] Benedetti-Panici P, Greggi S, Scambia G, Amoroso M, Salerno MG, Maneschi F, et al. Long-term survival following neoadjuvant chemotherapy and radical surgery in locally advanced cervical cancer. *Eur J Cancer* 1998;34:341 -6.
[23] Benedetti-Panici P, Greggi S, Colombo A, Amoroso M, Smaniotto D, Giannarelli D, Amunni G, et al. Neo-adjuvant chemotherapy and radical surgery versus exclusive radiotherapy in locally advanced squamous cell cervical cancer: results from the Italian multicenter randomized study. *J Clin Oncol* 2002;20:179-88.
[24] Centers for Disease Control Oral contraceptive use and the risk of ovarian cancer. *JAMA* 1983 *;* 249 :1596–9.
[25] Kyari O, Nggada H, Mairiga A. Malignant tumours of female genital tract in north eastern Nigeria. *East Afr Med J* 2004;81:142-5.
[26] Brinton LA, Bracken MB, Connelly RR. The incidence of chorio-carcinoma in the United States. *Am J Epidemio* 1986;123:1094-100.
[27] Shanmugaratnam K, Muir CS, Tow SH, Cheng WC, Christine B, Pedersen E, et al. Rates per 100,000 births and the incidences of choriocarcinoma and malignant mole in the Singapore Chinese and the Malays: Comparison with Connecticut, Norway, and Sweden. *Int J Cancer* 1971;8:165-75.
[28] Berkowitz RS, Cramer DW, Bernstein MR, Cassells S, Driscoll SG, Goldstein DP et al . Risk factors for complete molar pregnancy from a case-control study. *Am. J. Obstet. Gynecol 1985;* 152:1016–20.
[29] Kohorn EI . The new FIGO 2000 staging and risk factor scoring system for gestational trophoblastic disease: Description and critical assessment. *Int J Gynecol Cancer* 2001;11:73-7.
[30] Smith HO, Qualls CR, Prairie BA, Padilla LA, Rayburn WF, Key CR, et al . Trends in gestational choriocarcinoma: A 27-year perspective. *Obstet Gynecol* 2003;102: 978-87.

AUTHOR(S):
1. Dr. Anagha Kamath
2. Dr. Radha R. Pai

PARTICULARS OF CONTRIBUTORS:
1. Dr. Anagha Kamath,
   Assistant Professor,
   Department of Obstetrics and Gynaecology,
   Kasturba Medical College, Manipal University,
   Mangalore, India..
2. Dr. Radha R. Pai,
   Professor & Head of Department,
   Department of Pathology,
   Kasturba Medical College,
   Manipal University,
   Mangalore, India.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr.Anagha Kamath, Assistant Professor
Department of Obstetrics and Gynaecology, KMC,
Behind Leo Furnitures, Karangalpady,
Mangalore,India - 575001.
E-mail: anaghak23@gmail.com
Phone: +91 9880825793

DECLARATION ON COMPETING INTERESTS:
No competing Interests.

Date of Submission: **Jul 22, 2011**
Date of peer review: **Aug 02, 2011**
Date of acceptance: **Sep 07, 2011**
Date of Publishing: **Nov 11, 2011**