CANCER CERVIX ERADICATION DAY

CUTTACK, ODISHA, INDIA
Cancer Cervix Eradication Day

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Cancer Cervix Eradication Day

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Cancer cervix is the fourth most common cancer in women around in the world and leading cause of cancer death in under-developed country. Pap smear has been the gold strand screening test for cancer cervix since its introduction in 1949. New technologies are available to detect Human Papilloma Virus (HPV) infection, the main culprit for cancer cervix. Besides, potent vaccines against high-risk HPV are available which can prevent 70% of all cancer cervix. Evidences suggest that spreading awareness is lacking in our population.

With this background, we have decided to observe a day as world cancer cervix eradication day which will be a platform to educate and create awareness on cancer cervix. The breakthrough discovery “HPV infection causing cancer cervix” for which the Nobel Prize for physiology or medicine was awarded in 2008 to Dr. Harald zur Hausen, and subsequent availability of vaccine against HPV infection has encouraged us to think in the direction of cancer cervix eradication. We, therefore, thought that the birthday of Dr. Harald zur Hausen on 11th march would be the most appropriate day to observe world cancer cervix eradication day. Since 2011, we are observing world cancer cervix eradication day at Cuttack and spreading cancer cervix eradication massage- CARE i.e.

C : Create awareness to prevent early marriage , multiparity, multiple sex partners and to maintain good genital hygiene.
A : Avoid infection through HPV vaccination.
R : Regular Pap test.
E : Early diagnosis and prompt treatment.

In this 1st edition, the book has been thoroughly described, enlarged and updated with cancer cervix eradication awareness programme from 2011 to 2016.

Gratitude is expressed to the faculty members, both from India and abroad, who have sent in their valuable suggestions which have been given due consideration. We are sincerely thankful to our publisher, Newredmars Education. We are also deeply indebted to Nobel laurite Prof. Harald zur Hausen for his sustained support of this endeavour from its inception; his wisdom has made all the difference.

Healthy criticism and suggestions for further improvement of the book are solicited.

Niranjan Rout
Dean and Principal, AHRCC Cuttack Odisha
Since 2001, we have been organizing health education and awareness programmes for different diseases including Hepatitis B. We have been educating the common public in various ways like-distributing write-ups and leaflets, delivering radio talks, participating in television discussions, addressing public meetings and organizing health camps and speeding the message through both print and electronic media.

From 2007, we, the members of Ayur Bigyan.Com or ABC Foundation have been concentrating on creating awareness against cancer by different ways including educating public by organizing meetings, group discussions and radio talks. Also we are organising reorientation programmes for medical personnels through CMEs, Workshops and publishing articles in Journals.

In 2011, a group discussion was organised at Jagatsingpur, odisha in the month of March. The age of participants were between 46-76 years and male to female ratio was 3:1 .The educational qualification varied from Matric to M.A. A 45 minutes lecture on Cancer Cervix from etiology to prevention was delivered followed by question answer session. A questionnaire consisting of 10 questions related to cancer cervix were circulated among the participant before and after the lecture. It was observed that there was 87.5% improvement of knowledge among participants after group discussion and the participant expressed their desire to do pap test and accept HPV vaccine to prevent cancer cervix.

This observation provoked us to organise a programme on cancer cervix eradication.
The highlights of this programme were the presence of Dr. P.C. Mohapatra, President of Federation of Obstetricians & Gynaecologists of India (FOGSI) and Dr. N.C. Parija, President, Indian Association of Pathologists and Microbiologists (IAPM) and their deliberations and suggestions boosted us to continue our efforts.

As a part of this programme, we are -
1. trying to coordinate the activities of similar workers and organisations and recognising their work by honouring them in different fora.
2. trying to re-orient medical personnels regarding diagnosis, management and prevention of cancer cervix through CME, symposia, seminar, lectures, workshops etc.
3. trying to create awareness among people regarding the signs & symptoms of cancer cervix and the role of pap smear examination in early diagnosis of cancer cervix.
4. trying to create awareness among people that HPV infection is the main culprit for development of cancer cervix and a potent vaccine is available to prevent HPV infection.
5. trying to educate people to vaccinate their daughters against HPV infections and motivate mothers to do regular pap test for early diagnosis and treatment of cancer cervix.

We are aware that people all over the world are organizing such programmes in different ways in their own regions. Therefore, we have decided to observe “a day” as world cancer cervix eradication day during which we will try to co-ordinate the activities of similar workers and organizations with an aim to eradicate cancer cervix.

The break through discovery “HPV infection causes cancer cervix” for which the Nobel prize for physiology or medicine was awarded in 2008 to Dr. Harald zur Hausen, and subsequent availability of vaccine against HPV infection has encouraged us to think in the direction of cancer cervix eradication. We, therefore, thought that the birthday of Dr. Harald zur Hausen on 11th March would be the most appropriate day to observe World Cancer Cervix Eradication Day. On this day we will audit all our activities till date and will endeavour to coordinate activities of others in this field to create awareness for eradicating cancer cervix.

With the support and cooperation of all of you we want to spread the message - “Vaccinate daughters for HPV vaccine and motivate mothers for pap test screening”.

One day, like small pox, the cancer cervix will be eradicated from our globe.
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Introduction
Cancer cervix is the second most common cancer in women in the world and ranks 5th amongst all cancers in human. It contributes approximately 10% of worldwide tumour burden and up to 25% in developing countries. The table below shows the current burden of invasive cancer.

The alarming facts-
It is estimated that there occurs 493,000 new cases of cervical cancer occur each year, and 274,000 women die of the disease globally- majority are in developing world. In India 1, 32,082 new cases of cervical cancer occur each year and 74,118 women die of the disease

Every 7 minutes there is woman dying of cervical cancer- WHO report 2007.

Every sexually active woman is at risk of Cervical Cancer, throughout her life. 50-80% of sexually active women will acquire an HPV infection at some point in their life and up to 50% of these will be with an oncogenic HPV type. Young women are at a greater risk of HPV infection. Women continue to acquire new HPV infections, regardless of prior infection with the same or different HPV type. 80% cleared, but oncogenic types clear slowly or persist. And persistence of infection with high risk varieties leads to progressive pathology.

HPV DNA is seen in 95% of CIN and invasive cancers (Range 75-100%) 1, out of which HPV 16 in 60-65% and HPV 18 in 4-20%. HPV 18 is more commonly found in adenocarcinomas.

Risk factors of cervical cancer
Younger age at first intercourse, high number of sexual partners, high parity, low socioeconomic status, smoking and oral contraceptives, are significant risk factors for causation of cancer cervix. All of these, except smoking, however are linked to sexual behavior and HPV acquisition. HPV has been attributed as the principal sexually transmitted causal agent in
development of preinvasive and invasive cancer of cervix, as evidenced from etiological and epidemiological observations.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>India</th>
<th>Southern</th>
<th>Asia</th>
<th>World</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude incidence rate</td>
<td>26.2</td>
<td>21.5</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Age-standardized incidence rate</td>
<td>30.7</td>
<td>26.6</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td>Cumulative risk (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age period 0-64 years</td>
<td>2.5</td>
<td>2.2</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Standardized incidence ratio (SIR)</td>
<td>185</td>
<td>159</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Annual number of new cancer cases</td>
<td>132082</td>
<td>153535</td>
<td>493243</td>
<td></td>
</tr>
</tbody>
</table>

Rates are per 100,000 women.

Standardized rates have been estimated using the direct method and the world population as the reference.

Data sources: IARC, Globocan 2002

HPV is likely to be number 2 human carcinogen after tobacco. It causes 5% of human cancer, 10% of cancer in women, and 15% of cancer in women in developing countries.

HPV- HPV is a double stranded DNA virus having 8000 base pairs in length. The complete virion consists of a DNA core and a surrounding protein capsid. It has three major regions- two protein encoded regions (Early regions and late regions) and a non-coding upstream regulatory region (URR). The early region has six open reading frames (ORFs) - E1-E7 (E3 is absent). E5, E6 and E7 encode for oncoproteins. E1, E2 causes DNA replication, E6 inhibits p53, E7 inhibits pRb. Late region contains two separate ORFs named L1 and L2 that encode for viral capsid proteins. The URR regulates transcription from early and late regions and controls production of viral proteins and infectious particles.

Persistent infection with oncogenic HPV is the necessary cause of cervical cancer. But infection by HPV alone does not appear to be sufficient for causation of cervical cancer. There are some associated co-factors. A link between human leucocyte antigen (HLA) and HPV has been
explored. Interaction of HPV with histocompatibility antigen may explain why the same HPV type leads to invasive cancer in one patient but not in another.2

Nonenveloped double-stranded DNA virus.3

More than 100 types identified in human4 and one-third of them have been sequenced.30–40 anogenital4-5 and 15–20 oncogenic, 4-5. HPV 16 and HPV 18 types account for the majority of worldwide cervical cancers.6 Nononcogenic types - HPV 6 and 11 are most often associated with external anogenital. Genital tract HPV are classified by their relative malignant potential as Low-Risk, High-Risk and possible high-Risk oncogenic types.

1. Low oncogenic risk - 6, 11,40,42,43, 44, 53, 54, 61, 72, 73, 81.
2. High oncogenic risk - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82.
3. Possible high oncogenic risk - 26, 66, 73

Globally, the 4 most common ‘oncogenic’ HPV types are HPV 16, 18, 45 and 31.

Together, these account for ~80% of Cervical Cancer cases and HPV 16 and 18, alone, account for ~70% of Cervical Cancer cases.

Professor Harald Zur Hausen
He is a 2008 Nobel Laureate in Medicine or Physiology. He was recognized “for his discovery of human papilloma viruses causing cervical cancer”.2

Mechanism of HPV Transmission & Acquisition

• Sexual contact
  – Through sexual intercourse7
  – Genital–genital, manual–genital, oral–genital8-10
  – Genital HPV infection in virgins is rare, but may result from nonpenetrative sexual contact.8
  – Proper condom use may help reduce the risk, but is not fully protective against infection.5

• Nonsexual routes
  – Mother to newborn (vertical transmission)12
  – Fomites (e.g., undergarments, surgical gloves, biopsy forceps) 13-14

Hypothesized but not well documented; would be rare.

Most infected individuals are unaware that they are infected and may unknowingly spread the virus.
Pathogenesis of HPV infection

HPV virus enters at TZ after in or trauma of sexual intercourse. Part of HPV genome integrates in to host cell DNA- expression of E6 and E7 proteins. E6 binds with p53 tumour suppressor gene and induces p53 degradation. E7 binds with another tumour suppressor gene pRb (Retinoblastoma gene product) and inactivates this protein. Both p53 and pRb function in cell cycle control and act as regulators of cell proliferation, to prevent abnormal cell division. On interaction with high risk HPV E6 and E7 the regulatory path way of p53 and pRb is inactivated. E5 interferes with cell signaling through the EGF-receptor and disturb intercellular trafficking. These activities act as endogenous factors for development of premalignant and malignant lesions.

Diagnostic technique of HPV

Clinically, latent HPV infection is highly prevalent in general population. So diagnosis, particularly, of high-risk types is of great importance, as women carrying high-risk HPV infection have greater chance of developing cervical neoplasia. Conventional diagnostic technique of cytology, histology, and colposcopy cannot detect the viruses. Cellular changes of koilocyte detection are found only in 30% of cases. In colposcopy HPV infection can be detected as flat, papillary or inverting growth. So they are not of much help neither in detection nor prediction of HPV infection and associated outcome.

Molecular biologic technique is now commonly used for HPV diagnosis. They are
1. Tissue-in-situ hybridisation (TISH)
2. Filter In-situ hybridisation (FISH)
3. Southern Blotting (dot/slot blotting)
4. Polymerase chain reaction (PCR)
   - Traditional
   - Advanced
5. Hybrid capture system (HCS) from Digene Diagnostics
6. Fast HPV (Qiagen’s test) It tests-DNA of 14 types in < than 2.5 hrs, where No refrigeration is required. Cost will be < than $5 and the equipment does not require much space. This operated with battery and best suitable for field studies.

The FDA has approved the HPV DNA test to be used in combination with the Pap test to screen for cervical cancer in women over 30 years old. It does NOT replace the Pap test. Women in their 20s who are sexually active are much more likely (than older women) to have an HPV infection that will go away on its own. For these younger women, results of this test are not as significant and may be more confusing. For this reason, the HPV DNA test is not
recommended as a screening test in women under 30. The HPV DNA test is also used in women of any age who have slightly abnormal Pap test results to find out if they might need more testing or treatment.

“A single HPV-positive finding in a screening program must be not cause for alarm at any age, “An HPV-positive test should just be repeated after approximately 12 months, and only persistent infections should be investigated in depth. PCR assays should not be used in screening programs, because they detect too many harmless infections.”

**Prevention of HPV infection**
The only sure way to prevent HPV is to abstain from all sexual activity. Limiting the number of sex partners and avoiding sex with people who have had many other sex partners decreases a person’s risk of exposure to HPV. It is usually not possible to know who has HPV, and HPV infection is so common that even these measures do not guarantee that a person will not get HPV. Still, these measures may help reduce the number of times a person is exposed to HPV. Condoms provide some, but not total, protection against HPV. The virus can spread during direct skin-to-skin contact before the condom is put on, and male condoms do not cover the entire genital area, especially in women. The female condom covers more of the vulva in women but has not been studied as carefully for its ability to prevent HPV. Condoms are very helpful, though, in protecting from other infections that can be spread through sexual activity. Getting one of the HPV vaccines before being exposed to HPV will prevent some HPV.

**Treatment of HPV infection**
Treatments cannot cure HPV. But most genital HPV infections go away with the help of the body’s immune system. About 70% of HPV infections appear to go away within a year and 90% within 2 years. HPV itself cannot be treated, but the cell changes that come from an HPV infection can be treated. For example, genital warts can be treated. Pre-cancer cell changes caused by HPV can be found by Pap tests and treated. And cervical, anal, and genital cancers can be treated.

**Prevention of Cancer Cervix:**
Cervical cancer is preventable disease as most of its etiology is well known, but it yet to be prevented. Moreover the treatment result of this disease has not changed in last so many years. The screening programme for early detection is yet to be implemented in our country for all. The only answer is primary prevention of the dreaded disease by vaccination.**HPV – Vaccines- a major breakthrough**
2 Strategies are planned.
1. **Prophylactic Vaccines** - To prevent HPV infection and associated diseases
   a. Gardasil - Quadrivalent (6, 11, 16, 18) - MSD
   b. Cervarix – Bivalent (16, 18) – GSK

Prophylactic vaccines are designed to prevent HPV infection. This vaccine induces neutralizing antibodies against HPV capsid proteins L1 and L2. Both the commercially available contain hollow VLPs (virus like particles) assembled from recombinantly expressed major capsid L1 protein of HPV - morphologically similar to HPV, but they are harmless as they contain no DNA. On the other hand they have the ability to generate immune response, which is type specific and long term.

2. **Therapeutic Vaccines** – Under Research

The bright future of prophylactic vaccination.

Summary of two commercially available HPV vaccines.

Vaccination provides primary prevention against cervical HPV infection – a necessary cause of cervical cancer. HPV vaccines containing the most important oncogenic types (HPV 16 and 18) could prevent up to 70% of squamous cell Cervical Cancers and up to 85% of cervical adenocarcinomas.

Because vaccination does not protect against all oncogenic HPV types, screening must be continued.

Vaccination is given in a series of 3 doses over 6 months to girls and women.

**FOGSI & IAP recommendation**

HPV vaccine is not therapeutic. It does not treat existing HPV infection and CINs. Vaccinated women need to continue screening.

Target group - Bivalent 10-45 yrs and Quadrivalent 9-26 yrs, regardless of sexual debut.

Optimal age 12-16 yrs (before sexual exposure).

Routine vaccination – 10-12 yrs (IAP) The IAP recommends offering HPV vaccine to all appropriate females who can afford the vaccine.

Vaccination is not recommended in males at present.

Dosage - Bivalent 0,1,6 months IM, Quadrivalent 0,2, 6 months.

No booster - Follow-up studies over 5 yrs show persistent protection & good response to booster immunization indicating immune memory.

The vaccine should preferably be introduced to parents as a cervical cancer preventing vaccine and not as a vaccine against STI.

Screening programs should continue as per recommendations.
### Vaccines

<table>
<thead>
<tr>
<th>Vaccine Type</th>
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<th>Gardasil</th>
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<tbody>
<tr>
<td>HPV 16,18, VLP</td>
<td>HPV-6,11,18 VLP</td>
<td></td>
</tr>
<tr>
<td>L1 capsid component</td>
<td>L1 capsid component</td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>20μg HPV-16</td>
<td>20μg HPV-6, 40μg HPV-11</td>
</tr>
<tr>
<td></td>
<td>20μg HPV-18</td>
<td>40μg HPV-16, 20μg HPV-18</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>ASO4: 500μg aluminium Hydroxide, 50 μg 3 deacylated monophosphoryl lipid-A</td>
<td>Alum: 225μg aluminium hydroxyphosphate sulfate</td>
</tr>
<tr>
<td>Schedule</td>
<td>IM-0.1,6 months</td>
<td>IM-0.2,6 months</td>
</tr>
<tr>
<td>Target Population</td>
<td>Female 10-45 yrs</td>
<td>Females 9-26 yrs</td>
</tr>
<tr>
<td>Efficacy</td>
<td>100% against CIN2/3-5.5 yrs caused by 16,18</td>
<td>100% against CIN2/3-5 yrs caused by 16,18</td>
</tr>
<tr>
<td>Immunogenicity</td>
<td>• HPV-16-100% seroconversion, seropositivity remains &gt;5.5 yrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HPV-18-100% seroconversion, seropositivity remains &gt; 98% at 5.5 yrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HPV-45-100% seroconversion, seropositivity remains &gt;98% at 4.5 yrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HPV-31-100% seroconversion, seropositivity remains &gt;70% at 4.5 yrs</td>
<td></td>
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<tr>
<td></td>
<td>• HPV-16-100% seroconversion, seropositivity remains &gt;5.5 yrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HPV-18-100% seroconversion, seropositivity drops after 2 yrs</td>
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<tr>
<td></td>
<td>• Some evidence for activity against HPV 45, 31</td>
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Both vaccines do not protect against the serotype with which infection has already occurred before vaccination.

Counseling before vaccination

Optimal age for vaccination.

Recommended age: 11-12 yrs, with catch up age up-to 26 years (Advisory Committee on Immunization Practices-ACIP)

Clinical trials underway in women >26 years- found to be immunogenic, safe and effective in older women (up-to 55 years for Cervarix and 45 years for Gardasil).

Cervarix has recently been approved in Australia up to 45 years.

WHO position on HPV vaccines

The primary target population is likely to be girls within the age range of 9 or 10 through 13 years.

Clinical efficacy trials for both vaccines demonstrate that protection lasts for at least 5 years.

A need for booster doses has not been established.

FAQs

HPV testing before vaccination?

- No

Women with CIN?- protection against other subtype

Pregnancy - Not yet proved safe

Women planning to conceive- Defer
Become pregnant before completion?- postpone until delivery
MTP not indicated if conception does occur
Lactating mother?- Safe- as it is vaccine without live viral DNA
Immunocompromised patients-? No contraindication- immune response is less
Contraindication-Hypersensitivity to any vaccine component
Vaccinate in lying down position –observe 15 minutes
Side effects of vaccination
Local adverse effects -Pain (mild and moderate intensity) in 83%, swelling and erythema in 25% patients
Systemic adverse effects - fever reported in 4% of vaccines.
No serious vaccine related adverse events have been reported.
Conclusion
HPV is a necessary cause for cervical cancer. HPV-DNA testing can be included in screening programme- if financially feasible. Primary prevention (70-80%) can be achieved by vaccines- but to whom and when, how long the immunity lasts? - Unanswered till date. Though there are many unanswered issues before us, the vaccine is a boon and can be considered in young naive girls, so that we can prevent at least 70-80 % of cancer cervix. If we wait for the real result of its efficacy we will be wasting valuable time and many women will be suffering the dreaded disease which could have been prevented by simple vaccination. I wish the vaccine be implemented in national immunization programme?

Reference


Cytogenetic Changes in CIN and Carcinoma Cervix in Relation to HPV Infection

Sashmita Panda, Sagarika Samantaray, Niranjan Rout
Department of Pathology, Acharya Harihar Regional Cancer Centre, Cuttack.

Introduction:
Cancer cervix is the second most common cancer in females after breast cancer(I). Every year about one million women in the world suffer from this cancer and it causes 466,000 deaths per year. It is the most frequent neoplasm in India constituting 20% to 50% of all neoplasms(2,3). Every year more than 100,000 new cases of this cancer are reported in India(4). The mortality rate is also very high as cancer cervix ranks eighth among the killer cancers of females.

There are various risk factors responsible for the development of cancer cervix. They are sexual factors (pregnancy at young age, multiple sexual partners etc.), Multiparity, Smoking, Oral contraception, low socioeconomic status, oncogenes and tumor suppressor genes, immunodeficiency, chromosomal aberrations and infectious agents like chlamydia ‘trachomatis, Herpes viruses, HIV and Human papilloma virus.(S,6,7,B) On the basis of gross findings cancer cervix is divided into Exophytic tumors, Nodular tumors and ulcerative tumors.

On the basis of microscopic findings carcinoma cervix is broadly divided into squamous cell carcinoma and its variants (most common cancer of cervix) Adenocarcinoma and its variants, both of them constitute around 99% of all cervical cancers. Other rare variants are Neuroendocrine Carcinoma, different types of sarcomas and lymphoma . The spectrum of precancerous lesions of cervix are mild dysplasia (CIN-I), moderate dysplasia (CIN-II) and severe dysplasia or carcinoma in situ (CIN-III) which is also described now days on LSIL (CIN-I) and HSIL (CIN-II and CIN-III).

Role of HPV in the development of cervical carcinoma
Although there are many risk factors associated with the causation of cancer cervix, HPV infection plays an important role in the development of cervical cancer from precancerous lesions i.e. CIN
(Cervical intraepithelial neoplasia) to invasive carcinoma.\(^9\)

The infection with HPV virus may be transient or may cause early cervical lesions which regress spontaneously or progress to high grade lesions and eventually to invasive carcinoma.

HPV or Human Papilloma virus is a double stranded DNA virus with various subtypes. The different types of HPV found to be associated with cancer cervix are 6rll, t6 aild . 18. HPV types 16 and 18 are associated with about 70% of cervical carcinoma and major risk factor for progression of dysplasia to invasive carcinoma.\(^{10}\) HPV types 6 and 11 are generally found is condyloma accuminata and dysplasias. Few other high-risk types found to be associated with CIN II and CIN III are 30, 31, 33, 35, 39, 40, 43, 44, 45, 51, 52, 53, 56, 58 and 59. HPV DNA is present extrachromosomally in CIN cases whereas integration of viral DNA into the human DNA causes Invasive cal·cinoma. 20-40% of all sexually active women under 30 years of age have HPV infection. However, in majority cases it is self limiting. In 95% of CIN and invasive canters, HPV DNA is detected of which 60-65% has HPV 16. Adenocarcinoma are more commonly associated with HPV 18.

In India, 98-% of all the cervical cancer patients and 20% of the normal healthy women show HPV positivity.

Integration of HPV sequences along with progressive chromosomal changes mark the development of Invasive Cervical cancer. “the integration of HPV sequences either inactivates the tumor suppressor genes or activates the oncogenes to cause cervical carcinogenesis. Such integrations are cytologically manifested as gains, losses 2nd high copy number amplifications of chromosomal regions\(^{11}\). Thus HPV infection is considered as the most important risk factor for the development of cervical cancer.

Of the 15 high risk HPV types isolated from cervical carcinomas, HPV 16 is the most frequently detected, occurring in 50% of cervical cancers regardless of geographic origin.\(^{12}\)(13) The principal transforming proteins of high risk HPVs are E6 and E7, which block cell cycle exit in epithelial cells committed to differentiation, there by allowing viral replication. The major cellular targets of E6 and E7 are the P53 and Rb cell proteins respectively, which leads to negative regulation of cell growth.

HPV being an established agent in cervical cancer, development of HPV vaccine has become a dominant theme in contemporary HPV research. First human trial of HPV vaccine was reported from Card A (UK) in June, 1996. Recently phase and Phase II trials have been conducted in humans.
Cytogenetic changes and cancer cervix
The karyotype of malignant cells in cancer cervix appears to be complex and is not yet very clear. However, reports of association of cancer with chromosomal aberrations involving chromosome 1,3,4,5,6,11, and 17 are there(14).
Changes in chromosome 1 may result in acquisition of additional long-arm material, e.g. in the form of a 1q isochromosome. In chromosome 3, there may be additional material on 3q as has been shown by comparative genomic hybridization (CGH) in 90% of carcinomas. LOH (loss of heterozygosity) suggest that at least 2 genes of chromosome 4 are important, at 4p 16 and 4q 21-35. In chromosome 5, an isochromosome of 5p, often in two or more copies, is a frequent finding in cervical carcinomas and this is consistent with CGH (Comparative genomic hybridization) studies which shows amplification of 5p, usually in advanced stages. CGH (Comparative genomic hybridization) studies show a high frequency of loss in the region 6p 21-23-p25 of chromosome 6. Possible gene loss on both arms of chromosome 11 of cervical malignant cells are suggested by LOH (Loss of Heterozygosity) studies, at 11p 15 and 11q23. G-banding and LOH studies have shown the non-random loss of long arm of chromosome 17 (17q) where p53 gene is situated (at 17p 13.3).
Molecular genetics and cancer cervix
In the pathogenesis of cervical carcinoma there are three major components, two of them are related to the role of HPV (Human papilloma virus) ie the effect of viral E6 and E7 proteins and the integration of viral. DNA in chromosomal regions associated with well known tumor phenotypes; and the third component is the recurrent genetic alterations not linked to HPVYS) Recurrent loss of heterozygosity (LOH) have been detected in chromosome regions 3p 14-22, 4p16, 5p16, 6p21-22, 11q23, 17p13.3 without effect on p53, 18q 12-22 and 19q13, all of them suggesting the alteration of putative tumor suppressor genes not yet identified. The identification of specific genes involved, and their correlation with specific tumor properties and stages could improve the understanding and perhaps the management of cervical carcinoma.

References :


Unit-I

Group Discussion - A Method for Cancer Cervix Awareness

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Abstract
A group discussion was organised at Jagatsingpur, Odisha in March 2011. Eight members participated. The age group of participants was between 46-76 years and educational qualification varied from Matric to M.A. M:F ratio was 3:1.
A 45 minutes lecture on Cancer Cervix from etiology to prevention was delivered followed by question answer session.
Before lecture a questionnaire consisting of 10 questions related to Cancer Cervix were circulated and opinions collected. After the lecture & discussion another questionnaire consisting of 10 questions were circulated and opinions collected.
It was observed that there was definite improvement in the knowledge regarding Cancer Cervix awareness.
Post coital bleeding is one of the symptom to suspect cancer cervix. Before group discussion 85% of members were not aware of post coital bleeding. After group discussion 87.5% members expressed to go for pap test if there is postcoital bleeding.
It is now established that HPV is associated with cancer cervix. Before group discussion none of the members was aware of viral etiology of cancer cervix. After group discussion 87.5% of the member were aware of the role of HPV in causation of cancer cervix and opined that vaccine against HPV will prevent cancer cervix.
To conclude, such type of group discussion if carried out will definitely increase awareness against cancer cervix which will propagate the message of cancer cervix eradication.
Corroboration of findings in PAP smear, microbiological, serological tests and molecular diagnostic methods in female sex workers in west Bengal

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Objectives:
Correlation of findings on cervical cytology with serological, microbiological tests and PCR. Method: Papanicolaou, Gram stain, Chlamydia antigen detection, GC and Candida culture were performed on 162 cervical samples. Wet mount, Gram stain, Trichomonas vaginalis culture were performed on vaginal samples. Sera were subjected to HBsAg and HSV II IgM ELISA. HPV PCR was performed in 30 cases. Results: Findings on PAP were inadequate, 12.4% epithelial cells, 3% atrophic, 5% haemorrhagic, 18.5% inflammatory, MNGC - 0.6%, 15.4% reactive atypia, 3% metaplastic, 2.4% ASCUS, 13.5% LSIL, 3% HSIL, 15.2% koilocytes. HSV II ELISA was positive in 40.1%, HBsAg - 1.2%. Bacterial vaginosis + Candidiasis comprised majority of inflammatory smear, BV + Chlamydia were closely associated with ASCUS, TV was found in most cases with metaplasia and LSIL, Cases with koilocytes had other mixed infections. HPV PCR was positive in 70% of 30 cases, PAP smear in these showed - koilocytes -33.33%, reactive atypia-28%, LSIL -19%, HSIL- 4.7%, inflammatory - 10.27 %, keratin debris and anucleate squames - 4.7%. 63 samples were positive for HSV ELISA majority (22.2%) had reactive atypia in PAP smear, MNGC was found in 3.1 %. Conclusion: Findings mimicking ASCUS or LSIL can be due to coexisting other genital infections, as have been reported in other studies. While assessing HPV, all the cytologic features should be considered rather than koilocytes alone. Serology and PCR are useful complements to cytology.
Cancer cervix (squamous cell carcinoma) is the most common cancer afflicting Indian women. Early marriage, multiparity, low socioeconomic status, unhygienic condition and multiple sexual partners were earlier described as the etiological factors for development of cancer cervix. Now, it has been proved that these etiological factors facilitate infection by HPV (Human Papilloma Virus), the culprit for cancer cervix. Prof. Harald zur Hausen of Germany, in 1970, proposed that HPV infection causes cancer cervix, for which he was awarded the Nobel prize for medicine or physiology in 2008. Now, it is established that HPV infection, if not treated, takes a long incubation period of 8-10 years for a full blown case of cancer cervix.

A potent HPV vaccine, cervarix and Gradasil, is now available which can prevent the infection as well as the cancer. However, the vaccine is expensive, costing around Rs.20,000.00 for three dosage, which at present may not be feasible for vaccinating all teenage girls of our country. Further, the vaccine cannot prevent cancer in women who already have HPV infection of cervix. Inspite of the shortcomings, we can now think of how to eradicate cancer cervix. The possible modalities are - “Awareness”, “Vaccination” and, “Screen and Treat Approach”.

Awareness: Intensive and effective health education should be provided to all the women and girls. They should be educated:
1) To avoid early marriage and multiparity.
2) To avoid multiple sexual partners.
3) To avoid exposure to HPV infection.
4) To maintain good genital hygiene during reproductive life.

Vaccination: Though the vaccine is expensive efforts should continue to find ways to vaccinate all teenage girls so that
beneficial results can be reaped 15-20 years later.

**Screen and Treat Approach:** Adequate and clear communications between clinicians and pathologists and vice versa are necessary for better patient care and pap smear reporting.

From the period of the introduction of the pap smearing as a screening for cancer cervix during early 1950s up to present, the diagnostic terminology used to describe the cellular changes observed has undergone a gradual, unremitting series of changes due to a lot of inter and intra-observer interpretation. In course of time pap smear reporting has evolved from the Papanicolaou Classification (1950), through the Reagan’s Classification (1953) and the Richart’s Classification (1961) to the present the Bethesda System (TBS) described in 1988 and later modified in 2001. TBS is now the most widely accepted model for screening cervical smear and guiding clinical management.

Combined together the awareness for cancer cervix, vaccination against HPV, and the Screen and Treat approach, we can hope to achieve the goal of cancer cervix eradication like small pox and polio - from this world.
Abstract

It is now proved beyond doubt that cancer cervix is caused by Human papilloma virus. Out of the many high risk types of HPV, type 16 is demonstrated in more than 90% of cases of cancer cervix and that is the statistics world over. In a landmark study undertaken at AH Regional Cancer Center from Dec 2000 to Jan 2005, 100 women with cancer cervix and precancerous lesions were screened for HPV 16 by polymerase chain reaction. Out of these hundred women 56% were tested positive for HPV 16. Chromosomal profile of the same patients showed aberrant metaphases and the majority harboured more than one kind of aberration. Most of those tested positive for HPV 16 were poorly differentiated cancers, responded poorly to treatment and recurred early. On the whole HPV 16 positivity was a poor prognostic indicator.
1. Introduction

Cervical Cancer is the leading cause of morbidity, mortality among women in developing countries. As per GLOBOCON 2002, International Agency for Research on Cancer (IARC) data, more than 500,000 women are diagnosed & 270,000 deaths occur per year. Projections indicate that, by 2050, more than 1 million new cases of cervical cancer occur each year. Although prevention, early detection and treatment are established to be highly effective in controlling cervical cancer, unfortunately these are not optimally utilized especially in developing countries thus presents as a serious global problem. In the last decade or so it has been observed that the incidence is rising in younger population; a newer threat to the community. So there is an increasing demand for accuracy in diagnosis of its intraepithelial lesions, prevention, definitive treatment with negligible morbidity & preservation of fertility & sexual function.

In this chapter the newer developments in various aspects of carcinoma cervix have been precisely analyzed.

2. Recent advances in cytology screening

Traditional pap test has been successful in reducing the incidence of cervical cancer by 79% & mortality by 70% since 1950 but with a false negative rate of 49% in detecting cancer precursor lesions. Screening errors can occur at 3 stages: smear taking affecting smear sample quality, preparation of slide & interpretation.

To alleviate sampling & preparation errors newer techniques have been developed to provide more representative cell samples of evenly dispersed cells in a thin layer (mono layer) which aims to reduce material such as blood, pus and mucus from obscuring cells during cytological examination. The newer techniques are based on high speed video microscopy image interpretation software & field of...
view computers to analyze & classify the images of pap smear.

3. Liquid Based Screening (LBS):
Here cell sample collected is rinsed in a vial containing liquid preservative which transfers 80 – 90% of the cells to the liquid media as compared to 10 – 20% transferred to glass slide with conventional cytologic testing. It eliminates air drying & this newer technique reduces the rate of unsatisfactory smears of traditional pap test by 70 – 90%.

LBS devices include thin prep (cytyc corporation) & auto cyte prep (tripath imaging which is a computerized image processing device)

Thin prep Beta & thin prep 2000 processor have been the subject of most research studies completed to date. Another newer “Thin Prep 3000” technique processed the sample in a more faster rate.

4. Auto pap screening system:
This technique uses an automated microscope coupled to a special digital camera which scans the slide and uses computer imaging techniques to analyse each field of view on the slide. Computer algorithms are then used to classify slides as per abnormality. This technique reduces false negative rate by 32%.

5. Advances in hpv test for screening
Over the last decade, remarkable progress has been made in understanding Cervical Carcinogenesis. An overwhelming body of evidence shows that infection with various high risk Human Papilloma Virus (HPV) is the central & necessary cause for development of Cervical cancer & its precursor lesions. This fact was exploited for development of molecular technologies for viral detection to overcome the limitations of cytology as screening procedure. HPV DNA testing identifies women at risk for developing cervical neoplasia without the inherent subjectivity of Cytology. HPV Testing are being utilized as primary screening, triage of equivocal pap smears or AUSCUS and follow up after treatment for CIN.

HPV testing has a higher sensitivity & negative predictive value for detection of pre invasive disease than cytology. But it’s important drawback is lower specificity and low positive predictive value for high grade lesions. Outcome of HPV Test as a primary screening procedure (RCTs from Europe) states that there is definite reduction in incidence of high grade CIN, 3 to 5 yrs after screening. LSIL & ASCUS represent the largest fraction of abnormalities in cervical cancer screening.

The ASCUS-LSIL Triage study has investigated in a prospective, randomized fashion for the optimal management of LSIL & ASCUS by Immediate Colposcopy, HPV triage and repeat Cytology concluded that HPV triage
seemed to be at least as sensitive as immediate colposcopy in detection of high grade CIN, whereas need for colposcopy referral was halved. So HPV triage is the best strategy for management of women with ASCUS and this fact was incorporated recently in many international guidelines. HPV testing was also suggested to predict residual or recurrent CIN in women treated for high grade cervical lesions.

The 2 methods widely used for HPV detection are PCR and the Hybrid Capture II (HC 2, Digene Corp). HC2 is a nucleic acid hybridization assay for qualitative detection of DNA of 13 oncogenic & 5 benign HPV types. It is the only HPV test approved by Food & Drug Administration (FDA) for ASCUS triage and cervical cancer screening in combination with cytology after the age of 30 yrs. Among PCR techniques consensus PCR & type specific PCR are commonly used. Roche Amplicor HPV test is a commercial PCR based assay for HPV detection which involves a pool of 13 HR –HPV as included in HC2 assay. The most advanced HPV genotyping approaches are more appropriate for the identifications of individuals at risk of disease than its presence or absence. After consensus PCR amplification, HPV types can be discriminated by Reverse Hybridization with type specific probes. SPF PCR is a commercial INNO-LiPA HPV assay which is capable of genotyping 25 different HPV types. Among the most recent tests, HPV viral load, HPV Integration E2 status, HPV RNA detection (Pre Tect HPV Proofer) are promising for screening of cancer cervix for the future.

6. B. Biological markers of cervical neoplasia

Early detection and treatment of cervical precancerous lesions has the potential to improve patient outcome. A possible approach to the understanding of the mechanisms by which cervical carcinoma arises is to study protein expression of putative markers in cervical neoplasia of various histological risks. One way of achieving this goal is through the detection of cell cycle control proteins, the expression of which is modulated by HPV infection.

7. Proliferation Markers

pKi-67 is a large nuclear protein expressed in proliferating cells, which is
present in S, G2, M phase but is absent in
G0 & during DNA damage-induced cell
cycle arrest. This protein can differentiate
between normal squamous epithelium, atrophic epithelium & CIN III on the basis
of nuclear staining. Proliferating cell nuclear antigen (PCNA) has been used as a marker of cell proliferation although its practical value is limited owing to a lower specificity for replicating cells & fixation dependent immunostaining.

8. Cyclins
Regulation of the cell cycle depends on
the sequential activation & inactivation of
cyclin dependent kinases (cdks) through
periodic synthesis and destruction of
cyclins. Important functions of cyclins are
regulation of cell cycle, regulation of
transcription, DNA repair, differentiation &
apoptosis. In cervical squamous lesions, cyclin D1
expression is abrogated by high-risk but
not low-risk HPV infection, whilst cyclin
A and E expression is upregulated by both
groups of viruses. Moreover, cyclin B
expression is upregulated in high-grade
squamous intraepithelial lesions (CIN II,
CIN III) but not in low-grade lesions (CIN I, condylomata).
Recent work has revealed increased
expression of cyclin A & cyclin B and to
lesser extent cyclin E in glandular cervical
neoplasia.

A recent workshop under
the asuspicies of the RCOG reported that
cell-cycle control proteins show significant
promise as markers of oncogenic HPV
infection.

9. Cyclin - dependent kinase (CDK)
inhibitors
These markers block the kinase activity of
CDK(s) & subsequently prevent
phosphorylation of Rb gene family &
transition to S phase. Two groups of CDK
inhibitors have been identified, the p21 &
p16 family. p16 overexpression is observed in cervical
squamous intraepithelial lesions &
squamous cell carcinomas associated with
HPV indicating that suppressor function of
p16 can be overcome in the presence of
viral oncoprotein E7. Recently p16 has
been found to be a useful diagnostic
marker of cervical neoplastic squamous &
glandular lesions. In addition p16 may be
useful in the distinction between cervical
glandular intra-epithelial neoplasia (CGIN)
& benign mimics.
The role of p21 in etiology of cervical
carcinoma has not been well analysed.

10. Markers of apoptosis
10.1. bcl2: It is a proto-oncogene that is
located on chromosome 18 and encodes a
25-kDa protein. This extends cell survival
by blocking apoptosis. Immunohistochemical expression of bcl2
was observed in cervical tuboendometrioid
metaplasia but not in CGIN. Positive staining has also been found in a proportion of cervical adenocarcinomas suggesting that it may have a role in the evolution of these tumours through inhibition of apoptosis.

10.2. **p53**: Mutations of p53, a tumour suppressor gene, are the most frequent mutations encountered in human tumours. In cervical cancer, the presence of the p53 protein varies among different studies from a few percent to 62%. Accumulation of p53 is often the result of stabilization of p53 protein caused by mutations of the p53 gene. However, p53 mutation is uncommon in cervical neoplasia. Rather, p53 function is abrogated by the action of HPV E6 protein which binds to and inactivates p53.

10.3. **Heat shock protein (hsp27)**: It is a molecular chaperone which protects cells from various stresses. Recent data have shown that at a cut-off value of 40% for hsp27 expression, neoplastic cervical lesion could be identified from benign mimics with a sensitivity of 67.2% & specificity of 70% & with a positive predictive value of 82%.

10.4. **Minichromosome Maintenance Proteins (MCM)**: This protein plays an important role in eukaryotic DNA replication. Immunohistochemical studies of surgical material from the uterine cervix have shown that MCMs are ubiquitously expressed in cancer cells. Positive rate & level of MCM expression appeared to be higher in cancer cells than in normal proliferating cells of cervix & displastic cells suggesting that they may be useful diagnostic markers.

10.5. **Other markers of diagnostic utility**: Recent studies show the following markers have diagnostic importance

Carcino Embryonic Antigens (CEA) in cervical adenocarcinoma

Vimentin (VIM) in endometrial adenocarcinoma

Chromogranin A & Synaptophysin in cervical neuro-endocrine tumours

11. **Recent advances in diagnosis & staging of cancer cervix**

Traditional clinical staging system developed by FIGO is based on the belief that cervical cancer is a local disease & most of cases are from developing countries & surgical staging is not feasible with limited health care resources. In an attempt to improve clinical staging, lymphangiography, CT, USG & MRI are very useful but again the fallacy in the interpretation of results still persist. Querlece et al were the pioneers in the field of laparoscopic pelvic & aortic node sampling as a pre-radiation therapy evaluation of patients with cancer cervix. Laparoscopic staging is advocated in advanced cases & in patients when imaging shows positive and or bulky
lymphnode in early stages or negative para-aortic node in advanced stages. Laparoscopic lymph node sampling, lymph node aspiration for cytology, peritoneal biopsy and sentinel node identification are part of surgical staging for cervical cancer. It is feasible with minimal complications and short hospital stay. This will also help to avoid unnecessary extended field radiation in case of negative para-aortic nodes thus reducing morbidity. Laparoscopic staging in advanced or recurrent cervical cancer will help to select patients who will benefit from exenteration.

12. Role of sentinel node biopsy
The sentinel nodes are the first lymphnodes to receive lymph drainage from the primary tumour & most likely nodes to contain cancer if it has spread. The pathological status of the sentinel node reflects histopathology of the entire regional lymphatic drainage area in these cancers and determination of their pathological status may limit the extent of surgical treatment with reduction of unnecessary avoidable morbidity. It also avoids delay in commencing chemoradiation.

To identify the sentinel lymph nodes 2 tracer methods are used. The preoperative lymphoscintigraphy and intra-operative hand held gamma probe detection require the administration of the Technetium-99 in labeled colloid around tumour. The other method involves injection of Isosulfan blue dye around the tumour and the dye uptake by the sentinel node can be demonstrated during open or laparoscopic surgery. Laparoscopic detection of sentinel lymph node in cervical cancer is a feasible technique.

13. Positron emission tomography (pet) scan
Cervical cancers that take a lot of blood sugar are more resistant to treatment than those that are less glucose-hungry. Researchers also found that the high glucose uptake tumours can be identified by PET scan, which are already routinely used to determine tumour size and lymph node involvement.

PET scans monitor the amount of radioactive glucose tracer absorbed by cells, so the brightness of the image reveals how much glucose a tumour takes up. Moreover, PET scans can be used to determine the prognosis. PET is more accurate than the current standard i.e. C.T. in determining whether cervical cancer has spread to other areas of the body. This is an excellent tool to evaluate whether the patient has metastatic disease prior to surgery thus can avoid surgery if it is not appropriate. Though not 100% accurate it is the best tool available till date to help in determining which patients need surgery and which need radiation therapy.
14. Prevention of carcinoma cervix by HPV vaccination

Vaccination is among the most successful & least costly of all public health interventions. Primary prevention of cervical cancer can be achieved through prevention and control of genital infection with oncogenic H.P.V. types. Recent research on the safety and efficacy of candidate prophylactic vaccines against H.P.V. has shown nearly 100% efficacy in preventing persistent infections & development of cervical precancerous lesions. Two types of H.P.V. vaccines are currently being developed:

(i) Prophylactic vaccines to prevent H.P.V. infection & associated disease. These are 3 types but Bivalent (HPV 16,18) – Cervarix (MSD) & Quadrivalent (HPV 6,11,16,18)- Gardasil (GSK) are commercially available at present.

(ii) Therapeutic vaccines to induce regression of precancerous lesion or remissions of advanced cervical cancer. This vaccine can’t be considered as a primary prevention strategy because it targets existing lesions. This vaccine stimulates cytotoxic T lymphocyte (CTL) directed against cytotoxic epitopes derived from intracellular viral proteins. It is currently under research & expected to be in clinical practice in near future.

H.P.V. DNA free virus like particles (VLPs) are synthesized by self assembly of fusion proteins of the major capsid antigen L1 (or both L1 & L2) induce a strong humoral response with neutralizing antibodies. These are harmless as they contain no DNA but can generate type specific, long term immune response The following table also summarizes the characteristics of the two vaccines.

<table>
<thead>
<tr>
<th>Study feature of finding</th>
<th>Bivalent HPV-16 and HPV-18 VLPs (L1) capsid component only (Cervarix)</th>
<th>Quadrivalent HPV-6, 11, 16, 18 L1 VLP capsid component (Gardasil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expression system</td>
<td>insert cells (bucktails) 20 μg HPV 16, 20 μg HPV 18</td>
<td>Yeast 40 μg HPV 16</td>
</tr>
<tr>
<td>Concentration</td>
<td>580 A504 (preparatory)</td>
<td>20 μg HPV 6, 40 μg HPV 11, 60 μg HPV 16, 20 μg HPV 18</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>aluminum hydroxide adjuvants</td>
<td>aluminum hydroxide adjuvants</td>
</tr>
<tr>
<td>Dose, administration &amp; schedule</td>
<td>0.5 mL, IM, 0, 1 and 6 months</td>
<td>0.5 mL, IM, 0, 2 and 6 months</td>
</tr>
<tr>
<td>Storage &amp; Transport</td>
<td>Requires a cold chain system, stored &amp; transported at 2-8°C, should not be frozen</td>
<td>Requires a cold chain system, stored &amp; transported at 2-8°C, should not be frozen</td>
</tr>
<tr>
<td>Approved licenses as of Feb 2009 and WHO prequalification</td>
<td>Licensed in 92 countries WHO prequalified</td>
<td>Not commercialized</td>
</tr>
<tr>
<td>WHO prequalified</td>
<td>Licensed in 109 countries WHO prequalified</td>
<td></td>
</tr>
</tbody>
</table>

15. Recent advances in the treatment of cancer cervix

Over the years, various modalities from simple conization, radical surgery & new radiation methods to gene therapy are advocated in the management of cancer cervix. After years of research by pioneers...
world wide on the various surgical modalities of management in carcinoma cervix, the recent idea is towards acceptance of conservatism to get rid of both short term and long term morbidities & to reduce mortality. But the basic principles of proper pretreatment evaluation, surgical judgment & operative skill of the surgeon are important determinants of success.

(I) Non – antigenic – specific therapies
Topical application of interferon - α or β has been used with varying degrees of success, but after initial enthusiasm there has been no major interest in this type of treatment. On the other hand, antisense HPV – 16 E7 DNA oligonucleotides and inducible antisense HPV – 18 E7 or E6 messenger RNA (mRNA) have been used to inhibit growth of cervical cancer cell lines in vitro & invivo. Genetherapy offers some promising possibilities for recent future.

II. Gene therapy

Ex vivo approach to gene therapy
Ex vivo techniques involve removal of cells from the individual, manipulation of the cells in vitro and reinjection of altered cells. One approach is to remove tumour cells from a patient, insert genes in vitro to increase their immunogenicity and reinject them into the patient in order to obtain a systemic immune response that will recognize and destroy tumour cells.

In situ approaches to gene therapy
An exciting possibility is for the correction of specific molecular genetic abnormalities, responsible for carcinogenesis, to be corrected in tumour cells by replacing a normal copy of a tumour suppressor gene, such as p53, or suppressing expression of the product of an oncogene, such as K-ras. There is evidence that insertion of wild-type p53 and antisense K-ras into tumour cells with abnormalities of these genes suppresses tumourigenicity.

III. Intra-Operative Radiation Therapy (IORT)
This allows direct irradiation of a tumour bed during a planned surgical procedure. Irradiation is utilized to sterilize the remaining tumour nests after debulking of respective lesions. IORT allows direct visualization of the target volume which in turn results in a more precise mapping of the field to be irradiated. It also permits shielding of normal structures from radiation field. In this way, the total dose of radiation that can be delivered safely can be increased while diminishing radiation morbidity in normal tissue. It is seen that 15 Gy of IORT is equivalent to 30-45 Gy of fractionated external beam radiation.
IORT is delivered at the time of surgery, immediately following surgical resection. The radiation equipment is located within the space of the operating room. The dose of the IORT depends on the tumour burden after surgical resection, the depth of the target volume, the location of dose limiting normal structures (such as small bowel, the rectum & the bladder) & the degree of the previous irradiation in the patient. Painful neuropathy has been observed in 5-30% of patients. Other toxicities are GI tract related, ureteric obstruction, vascular and hematologic.

IORT allows maximizing local tumour control achievable with radiation, while minimizing the radiation exposure of dose limiting surrounding tissue. It has potential for improving both the long term local control and the overall survival in women with pelvic sidewall & / or para-aortic nodal recurrence.

Analyzing the results of various studies, it is found that higher five year disease free & overall survival rates are seen in women with microscopic residual disease when compared to those with gross residual disease.

IV. Conservative surgery

(a) Fertility Sparing surgery:

Daniel Dargent was the first person to advocate Radical Vaginal Trachelectomy (RVT) with pelvic lymph node dissection for stage IA2-IB1 and IIA which fulfills the needs for radicality along with fertility preservation. This procedure is combined with laparoscopic pelvic lymphadenectomy & parametrectomy.

Procedure of RVT

This procedure starts with infiltration of the vaginal epithelium using local anaesthetic agent with adrenaline & facilitates formation of vaginal cuff. A sleeve is formed by incising the vagina circumferentially approximately 2 cm distal to the cervix. Vagina is separated from cervix and adjacent structures by sharp dissection. Vesicovaginal space is further developed and bladder pillars identified. Blunt dissection of ureter is done cranially. The descending vaginal and cervical branch of uterine artery is ligated and divided. Posterior dissection is done by mobilizing POD. Uterosacral and cardinal ligaments are ligated and divided 1-2 cm from the cervix. Uterus is divided about 1 cm below isthmus & specimen subjected for frozen section to ensure cancer-free margin. Prophylactic circlage with single monofilament non absorbable suture is placed at the isthmus. Cervix is covered with vaginal flap.

Fertility outcome of RVT is quite encouraging. Combining various literatures out of 224 women, there were 96 pregnancies resulting 51 live births (53% live births). The disadvantages with
RVT is 50% preterm deliveries due to premature rupture of membranes.

(b) Laparoscopic ovarian preservation:
It is unnecessary to perform oophorectomy in young women as the incidence of ovarian metastasis is <1% in squamous cell carcinoma of cervix. Both ovaries should be transposed out of the future radiation field to preserve hormonal functions and if possible for fertility in young women. Recently laparoscopic laterocolic ovarian transposition is performed during laparoscopic lymphadenectomy or staging procedure.

V. Laparoscopic Assisted Radical Vaginal Hysterectomy (LAVRH)
Over last few years, there is a tendency for vaginal approach to the surgical treatment of cervical cancer after the advent of laparoscopic pelvic lymphadenectomy. This procedure combined with Schauta’s radical vaginal hysterectomy offers the potential for laparoscopic assisted treatment of early cervical cancer. Radical vaginal hysterectomy has many advantages over radical abdominal hysterectomy in terms of blood loss, transfusion requirement & hospital stay. LAVRH combines the advantages of minimizing surgical trauma with increased radicality & eliminating drawbacks of increased morbidity. In addition, the incidence of postoperative bladder and bowel dysfunction is low suggesting improved quality of life without compromising the survival.

Hertel et al analysed their own series of 200 patients and presented their data in 2003. After a median follow up time of 40 months, the overall 5 years survival is 83%, 18.5% patients experienced recurrence with 35% exclusively extrapelvic and 11% died of recurrence.

VI. Total Laparoscopic Radical Hysterectomy (TLRH)
Here the whole radical surgery is performed laparoscopically with an aim to decreasing morbidity in comparison to standard Wertheim’s hysterectomy.

VII. Nerve Sparing Radical Hysterectomy (Tokyo Method)
Although radical hysterectomy for early cervical cancer has a long history, Japanese gynecologist have made great efforts to revise classical Wertheim’s method so as to preserve pelvic autonomic nerves while maintaining a high curability (TOKYO METHOD). Japanese gynaecologists focused their attention on the cardinal ligament of the uterus rather than that of the parametrium. Once the pararectal and paravesical spaces are developed, the cardinal ligament appears clearly. They identified two parts, the vascular part and the neural part. The neural part is believed to contain pelvic splanchnic nerves and preserving this part does not hamper post operative bowel &
bladder function. They also advocated ureteric dissection without disturbing ureteric sheath.

**VIII. Role of Robotic surgery in cancer cervix.**

Robotic Surgery especially the da Vinci R System represents the most recent advancement in Minimally Invasive Surgery of this decade. The da Vinci R System was developed by Stanford Research Institute, USA Defence Dept and the National Aero-nautics and space administration in an attempt to allow Telesurgery for wounded soldiers. A surgical Robot is a computer–controlled device that can be programmed to aid the positioning and manipulation of surgical instruments intended to overcome the limitations of conventional Laporoscopy. The primary aim of Robotic Surgery is to help the surgeons to perform complex procedures laparoscopically rather than laparotomy. Robotic assisted Laporoscopy has features which overcome the difficulties of conventional Laporoscopy. The major advantage of Robot–assisted over Conventional Laporoscopy are–

**16. Mechanical Improvements**

Stabilization of Instruments within the surgical Improved ergonomics for Operating Surgeon Robotic assistance has been increasingly adopted in gynecology Oncology for Radical Hysterectomy with improvement in blood loss and recovery time over laparotomy although conventional Laporoscopy was rarely used for this procedure. In early stage operable Cervical Cancer, it is an superior device requires shorter time, less blood loss better retrieval of Lymph nodes with minimal morbidity and complications.

**17. Conclusion**

With vast advances in the field of prevention, early diagnosis and treatment of CIN, definitive treatment in different ages and stages, carcinoma cervix does not pose a serious threat to the community at present. Time is not far when “invasive cancer cervix” will remain as a history.

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A pilot study of HPV DNA and cytology testing in cervical cancer screening program

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Abstract
Persistent high risk human papillomavirus (HR HPV) infection is responsible for causation of more than 90% of cervical cancer. Lesions associated with HR HPV progress more rapidly to cancer than those not associated with it. Therefore detection of HR HPV is mandatory for treatment of cervical lesions. In spite of the facts, no studies have been done in this region of country about the prevalence of HPV related lesions. Hence this research project has been undertaken to find out the prevalence of HR HPV by detection of HPV DNA through PCR. To know the feasibility and to standardize the methods, a pilot study was done on a small sample size. The women above the age of 30 years attending the O&G OPD of S.C.B.Medical College, Cuttack were included in the study. Cervical cytosmear and cytology sample for HPV DNA detection were collected in aseptic method. Pap stained cytosmear was examined for detection of abnormal findings. The HPV DNA was tested by amplification and using consensus primers designed from the L1 region of the capsid protein of HR HPV. Out of 11 cases, only one case showed positivity for HPV DNA. The particular case was a 60 years old lady with squamous cell carcinoma of cervix. The HPV DNA detection by PCR is an important tool in increasing the sensitivity of pap smear examination. It can also aid in the management of cervical precancerous lesions.

Keywords: Cervical Cancer, HPV DNA, PSR.

Introduction:
Carcinoma of cervix is a significant global public health problem and is the second most common cancer among women with an estimated 493,000 new cases and 274,000 deaths occurring annually all over
the world. Current estimate indicates that every year about 5 lakh new cases of cancer cervix are diagnosed worldwide of which approximately 1.4 lakh cases occur in India. It is now learnt that about 75,000 women die due to cervical cancer in India, but in developed countries like USA, UK and Sweden the death rate is negligible. Recently WHO has classified carcinoma cervix as a preventable disease, Secondary prevention based on cervical screening has been successful in many developed countries. Screening helps in detecting pre-cancerous changes which if not treated may lead to development of cancer in future. Various tests used for screening of cancer cervix are:

Visual inspection of cervix with application of acetic acid.
Cervical cytology.
Demonstration of Human Papillomaviral antigens.

The widespread introduction of cervical screening by the Papanicolaou test, or Pap smear for cervical cancer screening has been credited with dramatic reduction in the incidence and mortality of cervical cancer in developed countries. Pap smear screening every 3–5 years with appropriate follow-up can reduce cervical cancer incidence by up to 80%. Though cervical cytology is an important tool for population screening program, the accurate sensitivity of cervical changes has been disappointing. It is considered by many as an important but imperfect screening method. Several recent meta-analyses have reported quite low pap smear sensitivity – in the range of 50% but as low as 20%. Decision makers should consider these findings highlighting the low pap sensitivity while making health policies.

Persistent HR- HPV infections are prerequisite for the development of cervical intraepithelial neoplasia (CIN) and cervical cancer. Women who have a positive HPV test may receive an additional test that will look for the presence of strains 16 and 18, as these are the two strains of HPV that have the highest risk of leading to cancer. Therefore, detection of HPV strains is mandatory for determining the course of disease and further management of the patients.

The study related to presence of high risk HPV in conventional cervical cytosmear, their follow-up and their correlation with HPV DNA detection in cytology samples are very few in this part of our country. Therefore this study can help us in screening of HPV in cervical lesions, subcategorizing the lesions into precancerous and invasive cancers and
also help in management of cervical lesions.

**Material and methods:**
With this rationale and background, a hospital based study was done in S.C.B. Medical College, Cuttack in collaboration with Regional Medical Research Center, Bhubaneswar. This was a pilot study to look for feasibility, prepare for the technique and pretesting the research tool, for the new data collection method. The pap smear was collected from all women who attend the Obstetrics and Gynecology OPD with the following inclusion criteria : patients above the age of 30 years with history of bleeding, excessive and / or foul smelling discharge per vaginum and also patients screened outside and suspected of having cervical lesions.

The transformation zone of cervix will be sampled by the Ayer’s spatula by aseptic method and the material will be transferred to a clean glass slide. The material for HPV DNA detection by PCR will be collected with the help of endocervical brush and will be dipped into a test tube containing phosphate buffer. It will be stored at -20°C till the test is carried out.

PCR is performed on extracted DNA using consensus primers designed from the L1 region of the capsid protein with sense primer: 5’CGT CCA AAA GGA TAC TGA TC3’ and anti sense primer: 5’GCA CAG GGA CAT AAC AAT GG 3’.

**PCR Amplification**
The reaction is carried out in a volume of 50 ul. It contains 250ng of each, sense and antisense primers, 0.2mM dNTPs, Taq buffer, 1.25 U of Taq polymerase, 5ul of sample DNA(100 ng) and the volume is adjusted with sterile distilled water. Positive and negative controls are also run in each experiment. Reaction is performed as per the following protocol:

Initial denaturation: 5min at 94°C; 35 cycles: Denaturation at 94°C (30sec), Annealing at 55°C (30 sec), Extension at 72°C (1 min).

The final extension step is carried out at 72°C for 5min.

Electrophoresis of amplified product (450bp) is run on 2% Agarose gel, stained with ethidium bromide, observed under UV transilluminator and the results are documented.

**Results:**
In the first phase we collected cervical cytosmears and cytology samples for HPV DNA from 11 patients. (Table 1)
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It included 4 cases of carcinoma cervix which showed features of squamous cell carcinoma in pap smear. After DNA amplification, test for HPV DNA was done with the sense primer and was found positive in one case. (Figure 1).

**Discussion:**

Human papillomavirus infection is now a well established cause of cancer cervix. High risk HPV types are detected in 99% of cervical cancer. Not all strains of HPV carry the same risk for cervical cancer. Of the 150-200 types of HPV known, 8-15 are classified as high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82), 3 as probable high-risk (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108). 6 Types 16 and 18 are generally acknowledged to cause about 70% of cervical cancer cases. Together with type 31, they are the prime risk factors for cervical cancer.7

Researchers have revealed that precancerous lesions of cervix associated with high risk HPV types progress rapidly to invasive cancer than those unassociated with it. Therefore the detection of DNA of high risk types of human papillomavirus bears significant role in management and prognosis of cervical lesions. With this in mind this mega study has been designed to study the prevalence of HR HPV in women of this region of country. Though a planning for including total 1000 females has been made, we started with only 11 females to look for the feasibility of the test and also to standardize it.

Out of 11 females from whom both cervical cytosmears and samples for HPV DNA were collected, there were 4 cases of squamous cell carcinoma, one case of high grade squamous intraepithelial lesion (HSIL) and one case each of carcinoma endometrium and ovary. Only one case of squamous cell carcinoma in a 60 years old lady showed presence of HR HPV DNA. Her pap smear also showed features of squamous cell carcinoma of large cell.

**Table 1**

(List of patients whose HPV-DNA was tested)

<table>
<thead>
<tr>
<th>Sl.No</th>
<th>Age</th>
<th>Clinical Diagnosis</th>
<th>Pap smear finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>28</td>
<td>Unhealthy cervix</td>
<td>Inflammatory smear</td>
</tr>
<tr>
<td>2.</td>
<td>70</td>
<td>Carcinoma cervix</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>3.</td>
<td>55</td>
<td>Ovarian tumour</td>
<td>Inflammatory smear</td>
</tr>
<tr>
<td>4.</td>
<td>60</td>
<td>Ca. endometrium</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>5.</td>
<td>45</td>
<td>Cervical erosion</td>
<td>Inflammatory smear</td>
</tr>
<tr>
<td>6.</td>
<td>60</td>
<td>Carcinoma cervix</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>7.</td>
<td>65</td>
<td>Carcinoma cervix</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>8.</td>
<td>75</td>
<td>Unhealthy cervix</td>
<td>HSIL</td>
</tr>
<tr>
<td>9.</td>
<td>87</td>
<td>Leukorrhea</td>
<td>Inflammatory smear</td>
</tr>
<tr>
<td>10.</td>
<td>52</td>
<td>Carcinoma cervix</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>11.</td>
<td>60</td>
<td>Carcinoma cervix</td>
<td>Squamous cell carcinoma</td>
</tr>
</tbody>
</table>

**Figure 1:**

450 bp

Amplification of L1 region of capsid protein

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keratinizing type. Even though no conclusive opinion can not be taken from such a small study, this shows that the prevalence of HR HPV is low. Hence it becomes still mandatory to continue this research work as this can affect the data collected so far relating to HRHPV prevalence and may affect the making of health policy by government about institution of HPV vaccination for public.

HPV Vaccine against Carcinoma of Cervix (HPV Vaccines) aims at primary prevention of carcinoma of cervix. The vaccines available are Bivalent (Cervarix) and Quadrivalent (Gardasil) HPV vaccine Types. In the Indian subcontinent more than 75% of cervical cancers are attributed to HPV types 16 and 18 implying that a high level of protection can be offered by these vaccines. Ideally vaccine should be administered prior to sexual debut. Indian Academy of Pediatrics (IAP) recommends that girls aged 10 to 12 years should be vaccinated. Vaccine can be administered up to the age of 26 years. Women remain at risk of infection throughout their sexually active lives and can therefore benefit from vaccination even up to the age of 45 years. Both the vaccines have demonstrated persistently high serum antibody levels and robust immune memories till 5-6 years after initial vaccination. The follow up of the vaccinated cohorts is on going process to see how long the protection lasts without booster doses. All vaccinated women should undergo cervical cancer screening as per the guidelines as these women are still susceptible to cervical cancer from HPV types not included in the vaccines.

References:


Abstract

Background: Cancer cervix is the second most common cancer in females after breast cancer and the mortality rate is also very high as cancer cervix ranks eighth among the killer cancer in females. After Papanicolaou introduced pap smear in 1949, it is the gold standard test for screening and detection of cervical cancer.

Methods

The cervical smear from AHRCC, Cuttack were studied over a period from Jan 2010 to Dec. 2010.

Results

Out of 1130 pap smears, 8 were inadequate smears. Inflammatory constitute 553, carcinoma present in 417 smears, radiation changes seen in 11 cases suspicious cells found in 117 cases and 4 cases exhibited post RT granulomatous changes. CIN seen in 5 cases, no evidence of malignancy seen in 5 cases.

Conclusion

Pap smear is highly effective and most successful test in diagnosing cervical cancer and for post op. follow up for recurrence.

Introduction

Worldwide cancer cervix is the second most common cancer in females after breast cancer(1). Every year about one million women in the world suffer from this cancer and it causes 466,000 deaths per year. It is the most frequent neoplasm in India constituting 20% to 50% of all neoplasms(2,3). Every year more than 1,00,000 new cases of this cancer are reported in India(4). The mortality rate is
also very high as cancer cervix ranks eighth among the killer cancer of females. In general higher, incidence are found in developing countries contributing 83% of reported cases annually, where as developing countries add only 3.6% of new cancers(5). Early detection and treatment of precancerous lesions can prevent progression to invasive cervical cancer. Pap smear is the most efficient and very easy to do screening test for the detection of suspicious smears or premalignant lesion, cancers and for post op. or post-radiation follow up for evidence of recurrence of the cancer. Pap smear is the most efficient and very easy to do screening test for the detection of suspicious smears or premalignant lesion, cancers and for post op. or post-radiation follow up for evidence of recurrence of the cancer.

The Bethesda system (2001) for the reporting of pap smear classifies squamous cell abnormalities into four categories (1) ASC (Atypical squamous cells): two subcategories: “ASC-US” (atypical squamous cells of undetermined significance) and “ASC-H” (atypical squamous cell can’t exclude HSIL), (ii) LSIC (low grade squamous intraepithelial lesion, (iii) HSIL (High grade squamous intraepithelial lesion and (iv) squamous cell carcinoma.

Our aim is to detect the prevalence of cervical cancer and their post op./post RT follow up.

Material and Methods

Cervical smears were studied in the Dept. of Pathology, AHRCC, Cuttack over a period from Jan 2010 to Dec. 2010. Age and clinical details of patients were recorded. Slides collected in the Gynaec Department were received and pap smear was done. The slides were examined light microscopically by the cytopathologist and the results were recorded. On analysis of observations were made and compared with clinical presentation.

Results

Out of 1130 pap smears studied, 8 cases (0.7%) were inadequate smears. 553 (48.93%) cases were inflammatory smears which constitute the largest group. Suspicious cells were found in 117 (10.35%) cases. Carcinoma constitute 419 (36.89%) cases out of which most common were squamous cell carcinoma 401 935.57% cases. Followed by poorly different cancer 13 (1.15%) cases only 2 cases (0.17%) of Adeno Carcinoma were found. Radiation changes were seen in 11 (0.97%) cases and post. RT. Granulomatous changes seen in 9 (0.35%) cases. CIN and normal squamous cells reported in 5 (0.44%) and 8 (0.7%) cases respectively. 1 case (0.17%) each of sarcoma vault and carcinoma endometrium were reported. No evidence of malignancy seen in 5 (0.44%) cases.

Highest number of cases are between 41-50 age group. Maximum number of cases were cancer and post operative or post radiation follow up cases. This is probably
because AHRCC is the Tertiary cancer centre.

Discussion

Cancer cervix is one of the leading cause of cancer death among women in developing countries. The conventional pap smear method has helped reducing the cervical cancer incidence and mortality rates roughly half to two thirds, since its introduction in 1949 by George Papanicolau.(6)

There are various risk factors responsible for the development of cancer cervix. They are sexual factors (pregnancy at young age, multiple sexual partners etc.), multiparity, smoking, oral contraception, low socioeconomic status, oncogenes and tumour suppressor genes, immunodeficiency, chromosomal aberrations and infections agents like chlamydia trachomatis Herpes virus, HIV and human papilloma virus(7,8,9,10). On the basis of gross findings cancer cervix is divided into exophytic tumours and ulcerative tumours.

On the basis of microscopic findings carcinoma cervix is broadly divided into squamous cell carcinoma and its variants (most common cancer of cervix) Adenocarcinoma and its variants, both of them constitute around 99% of all cervical cancers. Other very rare variants are neuroendocrine carcinoma, different types of sarcoma and lymphoma. In our study we found 402 cases of squamous cell carcinoma, only 2 cases of adenocarcinoma and 13 cases of poorly differentiated carcinoma.

Radiation induced changes found in 11 cases which should not be confused with recurrence. Most of the cases were inflammatory smears (98.93% cases). Carcinoma cervix is preceded by a prolonged premalignant phase. Therefore, determination of stage of the disease process is very essential for proper clinical management. For this most common method used is conventional pap smear examination. It has been decided internationally that every women above the age of 30 years most have at least one pap smear examination. It is also very essential for the post operative cancer cervix and post radiation follow up to rule out recurrence of the disease.

References


A 72 years old grandmother of six children diagnosed and treated case of carcinoma cervix presented in our OPD on March 2012 for her regular follow up. She was asymptomatic and general examination was essentially normal excepting her age related weakness. Gynecological evaluation including a per speculum, per vaginal examination showed no abnormality and she was declared to be clinically controlled. Her OPD registration numbers in A.H. Regional Cancer Centre, Cuttack revealed that she first presented in February 1985 and a bunch of old but neatly tagged OPD papers were an evidence of a stringent and rigorous follow up.

Looking back to her file and past records of 27 years, we found that she had initially presented in February 1985 as a perimenopausal female of 45 years with irregular bleeding per vagina, pain in lower abdomen and occasional post coital bleeding. A physical examination done then showed moderate pallor, no icterus cyanosis, clubbing or lymphadenopathy, abdomen was soft, nontender and there was no organomegaly. Per speculum and vaginal examination showed a large ulceroinfiltrative, friable growth over the cervix extending to lower 3rd of the vaginum with foul smelling discharge, bilateral parametrium were medially infiltrated with disease, not extending to the lateral pelvic wall. With a clinical diagnosis of carcinoma cervix FIGO stage IIIA she had been referred to the department of Gynecology for tissue diagnosis and confirmation. Histopathology (HP) showed moderately differentiated squamous cell carcinoma of uterine cervix and she had been referred
back to Radiation Oncology for further management.

With a confirmatory diagnosis of Carcinoma Cervix Stage-III A she was planned for radiotherapy and received radiation to the pelvis using telecobalt machine with Co-60 radioactive source in AP/PA portals to a dose of 50Gy/25# from 22ndFebruary1985 to 29th March 1985. A single fraction of low dose brachytherapy was given after completion of external radiotherapy using caesium 137 to a dose of 20 Gy prescribed to point A whereby the entire treatment was completed within a period 6 weeks. She tolerated treatment fairly well with acceptable skin, mucosal toxicities.

Carcinoma cervix is the most common cancer among females in India and is the leading cause of morbidity and cancer related deaths. (1) The recommendations of NCI (National Cancer Institute), USA for the treatment of carcinoma cervix came much later in 1999. In February 1999, NCI gave an alert that “strong consideration should be given to chemoradiation in all patients with locally advanced carcinoma cervix” (2) NCI, USA further concluded that platinum based chemotherapeutic agent should be the drug of choice for carcinoma cervix. (2) In December 1999, NCI made a statement that “For every 1 day protraction of treatment beyond a period of 8 weeks in carcinoma cervix, locoregional failure increases by 1%”. (2)

Although these guidelines were not known then, her records reveal a judicious treatment protocol and a stringent follow up for the last 27 years. Treatment of cancer is a challenge for the physicians and a battle for survival for the patients. This lady has fought the odds with tremendous courage and strength and her experience needs to be shared amongst all cancer patients particularly females who succumb to this dreadful disease due to lack of both knowledge and awareness. This long term survivor of 27 years of carcinoma cervix is testimony to the fact that cancer is curable and a rigorous follow up in these patients is as important as the treatment itself.

References:
Aim of the study

The aim of the study was to evaluate the effect of socioeconomic status (SES) on women having Cervical Cancer in Odisha.

Methods

Data were obtained from 44 patients being diagnosed between January 2012 to March 2012. Social class is determined on the basis of three parameters of development, namely education, occupation and income. Education determines the knowledge, attitude, and value system of individuals and their socioeconomic growth potential. Occupation determines the income generating capacity of individuals and their status. Income determines the purchasing power of individuals and their socioeconomic status. On the basis of these parameters populations are divided into social classes - upper, upper middle, middle, upper lower and lower. These social class gradients have helped to provide a deeper understanding of clinical phenomena. The patients those came at A.H.R.C.C for check up were asked about their annual income, property, basic education, type of food taken daily, quantity and quality of food etc and then they were put into their perspective categories.

Results

As a whole most of the patients belonged to upper lower class those came at A.H.R.C.C, Cuttack. Cervical cancer risk is associated with a low socio-economic status (SES).
Impact of obstetrics and gynecology history of women on Cervical Cancer in Odisha

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Department of Pathology, Acharya Harihar Regional Cancer Centre, Cuttack.

Aim of the study
The aim of the study was to determine the impact of obstetrics and gynecology history of women on Cervical Cancer epidemiology in Odisha and to evaluate the importance of gynecological health and hygiene in prevalence of cervical carcinoma in poor sectors of society.

Methods
A prospective analysis of 44 patients were taken in Outdoor Patient Clinic and had cytological confirmation of Carcinoma Cervix in Department of Pathology, AHRCC, Cuttack.

Results
Women were recruited from outpatient gynecology clinic and 98% of them were screened positive for Squamous Cell Carcinoma of cervix, rest 2% was found positive for Adenosquamous Carcinoma of Cervix. The clinical extent of the disease was classified according to FIGO system. There were 4 (9%) patients in stage IB, 14 (31%) patients in stage IIB and 26 (59%) patients in stage IIIB. They were preferentially housewives (p<0.001), began sexual life early, had a greater number of pregnancies (p<0.001), number of deliveries (parity from 1 to 8) and only 2 (4%) faced abortions. Besides, most of them belong to upper lower class and have low literacy level(p<0.001).

Results
Patients attending the hospital had lower education level (p<0.0001), age at menarche(11-16)years and age at menopause(38-54)years. They were preferentially housewives (p<0.001), began sexual life early, had a greater number of pregnancies (p<0.001), number of deliveries (parity from 1 to 8) and only 2 (4%) faced abortions.
Dr. George Papani Colaou is said to be the **father of Cytology** since he could detect first Cancer cells in the vaginal smear of Cancer Cervix, patient in 1923. After long years of his continued work he could be able to publish **“New Cancer diagnosis”** in which the importance of Pap smears test was mentioned in detail. Then the Pap. Test won acceptance and became a routine practice for screening Cancer Cervix patients world wide, specially the Western world. George Papani Colaou became the savior of society for his discovery to save innumerable patients from cancer by way of early detection and treatment. On the basis of his research and persistent spirit of scientific discovery professor Harald Zur Haussen found out the real cause of cancer cervix and won noble prize in medicine for his discovery – HPV (Human Papilloma Virus) - the cause of cancer cervix. The things have evolved step by step and now, we are able to find out vaccine against HPV, the cause of cancer cervix. In due course, the HPV Vaccine will be widely used to eradicate Cancer Cervix from the face of the world like Small pox and Polio.

The Western World had widely practiced HPV Vaccine among young girls to prevent Cancer Cervix where as India lags behind. Let us create awareness about this and know how HPV Vaccine prevent cancer Cervix.

The human papilloma virus (HPV) vaccine prevents infection with certain species of human papillomavirus associated with the development of cervical cancer, genital warts, and some less common cancers. Two HPV vaccines are currently on the market **Gardasil** and **Cervarix**.

Both vaccines protect against the two HPV types (HPV -16 and HPV-18) that cause 70% of cervical cancers, 80% of anal cancers, 60% of vaginal cancers, and 40% of vulvar cancers. These HPV types also cause most HPV induced oral cancers, and some other rare genital cancers. Gardasil also protects against the two HPV types
(HPV -6 and HPV -11) that cause 90% of genital warts.

Both vaccines have been shown to prevent potentially precancerous lesions of the cervix. Gardasil has been shown to prevent potential precursors to anal, vulvar, vaginal, and penile cancers. HPV vaccines are expected to protect against HPV induced cancers of these areas as well as HPV induced oral cancers.

The World Health Organization (WHO), as well as public health officials in Australia, Canada, Europe and the United States recommend vaccination of young women against HPV to prevent cervical cancer, and to reduce the number of treatments for cervical cancer precursors. Worldwide, HPV is the most common sexually transmitted infection in adults. For example, more than 80% of American women will have contracted at least one strain of HPV by age fifty.

Although most women infected with genital HPV will not have complications from the virus, worldwide there are an estimated 529,000 new cases of cervical cancer and 275,000 deaths per year. About 85 percent of cancers, and eighty percent of deaths from cervical cancer occur in developing countries. In the United States, most of the approximately 11,000 cervical cancers found annually occur in women who have never had a Pap smear, or not had one in the previous five years. HPV is also the cause of cervical intraepithelial neoplasia (CIN). CIN is a precursor to cervical cancer, and is painful and costly to treat. It is not known how many women worldwide are diagnosed with CIN. Since the vaccine only covers some high-risk types of HPV, experts still recommend that women get regular Pap smear screening even after vaccination.

HPV vaccination is approved for use in males in many areas. In addition to protecting their partners from cervical cancer, vaccination can protect males against anal cancer, and may prevent other HPV associated cancers. Gardasil can also protect males against genital warts. HPV vaccination has been recommended for males in USA where vaccine uptake among women has been low. Vaccination is also recommended in populations at higher risk for HPV associated cancers, such as men who have sex with men and those with compromised immune response.

In this connection, we doctors, paramedical workers, NGO’s and elited public should create awareness about the importance of cancer, its early detection by pap test and encourage taking HPV vaccine among high risk persons of cancer cervix.
Abstract
The two primary means of obtaining and diagnosing cervical dysplasia are the conventional Pap smear and the liquid-based thin layer preparation. Although the data are conflicting, it appears that liquid-based cytology may be superior to conventional cytology, increasing detection rates of low- and high-grade abnormalities. The current recommendation is to start cytologic screening within 3 years after the onset of sexual activity or when a woman reaches the age of 21. The American Cancer Society (ACS) recommends annual screening until age 30 with conventional Pap smear or every other year if liquid-based cytology is used. If a woman has two to three normal smears, the screening interval can be lengthened to every 2 to 3 years. High-risk women should be screened annually. ACS recommends stopping at age 70 if there have been three consecutive negative smears in the past 10 years.
Background: Cervical cancer is the most common gynaecologic cancer in women and is the leading cause of cancer death in women in under developed countries. Invasive squamous cell carcinoma of cervix. is the end stage of a disease process beginning with atypical transformation of cervical epithelium at squamo-columnar junction le:ading to cervical intraepithelial neoplasia of advancing erades and eventually invasive carcinoma. For over 60 years since its introduction in 1949, papanicolaou smear has been the gold standard as screening test for cervical cancer.

Methods: The cervical smears from Depmtment of Pathology, SCB Medical College, Cuttack were studied over a period from June 2010 to July 2011. The samples were collected from the uterine cervix and stained according to methods of Papanicolaou.

Results: Out of 337 pap smears, 81 were inadequate smears. From 1256 adequate smears, Atypical squamous cells of undetermined significance (ASCUS) accounted for 8 cases (0.6%), squamous intraepithelial lesions (LSIL & HSIL) constituted 5.38%. Atypical glandular cells of uncertain significance (AGUS) constituted 0.44% and 13 cases (0.97%) were found to be neoplastic (Squamous cell carcinoma - 9 cases and Adenocarcinoma - 4 cases). Subsequence histopathological examination was done for correlation of cytologic findings.

Conclusion: Conventional pap smears are effective in reducing morbidity and mortality from carcinoma of cervix by detecting preinvasive lesions. It is the most successful cancer screening test in the history of modern medicine.

Keywords: Squamous intraepithelial lesions, cancer cervix, pap smear.
Cervical Cancer is the leading cause of morbidity, mortality among women in developing countries. As per GLOBOCON 2002(IARC) data, 500,000 women are diagnosed & 270,000 deaths occur per year. Projections indicate by 2050, more than 1 million new cases of cervical cancer will be there each year. Although Prevention, early detection and treatment are established to be highly effective in controlling cervical cancer, unfortunately these are not optimally utilized in developing countries. So, the reality about this cancer is though preventable but not yet prevented. The objective of Cervical cancer screening is to prevent the occurrence of Invasive Cervical Cancer by detecting in pre-invasive stages. Screening tests like traditional Pap tests, Liquid based Cytology, Visual Inspection with Acetic Acid (VIA) and Lugols Iodine (VILI) and HPV testing though have their own pros & cons but if conducted in a proper way have optimal accuracy in detecting CIN, early asymptomatic preclinical invasive cancer. Effective therapy like Cryotherapy, Laser Ablation and Conisation, Loop Electrosurgical Excision Procedure (LEEP), Cold knife Coagulation are widely available to tackle these Precancerous conditions. Pap test still remains to be most practical, effective, fairly sensitive and quite efficient to pinpoint the suspicious group in which further evaluation is required. Its role in mass screening is unquestionable. Colposcopy is a most useful aid to triage women with positive tests, to assess the nature and extent of precancerous lesions & guide to take biopsy from exact side whenever needed. The overall accuracy for detection improves maximum if cytology and colposcopy are simultaneously combined. It is well told “Cytology discovers the crime and Colposcopy locates the culprit”.

“The first observation of Cancer cells in a smear was the most thrilling experience of my scientific career”.

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Dr George Nicholas Papanicolaou, 1928

From the era of Papanicolaou who was nominated for Nobel Prize to H Z Hausen, who received nobel prize in the yr 2008 for his work on HPV, there has been a lot of innovations, changes and modifications in the field of screening of Cancer Cervix. It was Dr Papanicolaou who first spread the concept of Cervical smear

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considered as father of Modern Cytology.
In 1941, his research work published in
*American J of Obstet. & Gynecol* titled
“Diagnosis of Uterine Cancer by
Vaginal Smear” created a lot of
enthusiasm among various workers
worldwide in the field of screening.
Traditional Pap test has been successful in
reducing the incidence of Cervical Cancer
by 79% and mortality by 70% since 1950
but with a false negative rate of 49% in
detecting cancer precursor lesions.
Screening error can occur in 3 stages:
Smear taking affecting smear quality,
Preparation of slides and interpretation
by cytologists. To alleviate sampling and
preparation errors newer techniques have
been developed to provide more
representative cell samples of evenly
dispersed cells in a thin layer (monolayer)
which aims to reduce material such as
blood, pus and mucus from obscuring cells
during cytological examination. The newer
techniques are based on high speed video
microscopy image interpretation software
& field of view computers to analyze and
classify images of Pap smear. Among
these *Liquid based screening* (LBS)
including Thin Prep (Cytyc Corporation)
& Auto Cyte Prep (tripath imaging which
is a computerized image processing
device) have gained much popularity in the
developed world. Liquid based Cytology
transmits 80-90% cells to the media,
eliminates air drying. It reduces the rate of
unsatisfactory smears of traditional pap
test by 70% to 90%. LBS has been used by
90% gynaecologists in United States since
2003.
Over the last decade, remarkable progress
has been made in understanding Cervical
Carcinogenesis. An overwhelming body of
evidences show that infection with various
high risk Human Papilloma Virus
(HPV) is the central and necessary cause
for development of Cervical Cancers & its
precursor lesions. This fact was exploited
for development of molecular technologies
for viral detection to overcome the
limitations of Cytology as screening
procedure. *HPV DNA testing* identifies
women at risk for developing cervical
neoplasia without the inherent subjectivity
to cytology. HPV test can detect HPV
DNA in exfoliated cervical cells which can
detect about 100% Invasive Cancers, 75-
90% precancerous lesions (LSIL,CIN,HSIL)
and 50% equivocal smear (ASCUS). Various
HPV testings are being utilized as primary screening, triage
of equivocal pap smears or ASCUS and
follow up after treatment of CIN.
HPV Testing has a higher Sensitivity and
negative predictive value for detection of
pre-invasive disease than cytology. But its
important drawback is lower specificity
and low positive predictive value for high
grade lesions. Outcome of HPV test as a
primary screening procedure (Various RCTs from Europe) states that there is definite reduction in incidence of high grade CIN ,3 to 5 yrs after screening .LSIL and ASCUS represent the largest fraction of abnormalities in cervical cancer screening. The **ASCUS-LSIL Triage study** has investigated in a prospective ,randomized fashion for optimal management of LSIL and ASCUS by immediate Colposcopy ,HPV Triage and repeat cytology concluded that HPV Triage seemed to be at least as sensitive as immediate colposcopy in detection of high grade CIN ,where need for Colposcopy referrals was halved. So HPV triage is the best strategy for management of women with ASCUS and this fact was incorporated recently in international guidelines. HPV Testing was also suggested to predict residual or recurrent CIN in women treated for high grade cervical lesions.

The two methods widely used for HPV detection are **PCR** and **Hybrid Capture II** (HC,Qiagen,Digene Corp). HC2 is a nuccic acid hybridization assay for qualitative detection of DNA of 13 oncogenic(Probe A) and 5benign(Probe B) HPV types in clinical specimen. It is the only HPV test approved by Food & Drug Administration (FDA ) for **ASCUS triage** and cervical cancer screening in combination with Cytology after the age of 30 yrs. Among PCR techniques **consensus PCR** and **type specific PCR** are commonly used. Roche Amplicor HPV test is a commercial PCR based assay for HPV detection which involves a pool of 13 HR -HPV as included in HC2 assay. The most advanced HPV Genotyping approaches are more appropriate for the identification of individuals at risk of disease than its presence or absence. After consensus PCR amplifications, HPV types can be discriminated by **Reverse Hybridization** with type specific probes. **SPF PCR** is a commercial INNO –LiPA HPV assay which is capable of genotyping 25 different HPV types. Among the most recent tests, HPV Viral Load, HPV integration E2 status ,HPV RNA detection (Pre Tect HPV Proofer) are promising for screening of Cancer Cervix for the future. Outcome from translational research also identifies markers that reflect dysregulation of cell cycle in cervical neoplasia such as **p 16, Ki -67 ,MCM Proteins and Cyclin E** which are expected to be included in screening of Cancer cervix in future.

**References**

Abstract

Objective: To study the various histopathological spectrum of cervical lesions in Dept of Pathology, S.C.B medical college over last 4 years.

Material and Methods: A retrospective analysis of 2575 cervical lesions diagnosed in Dept of Pathology, S.C.B.Medical College, Cuttack was done from Jan 2008 to Dec 2011. Cervical lesions were divided into inflammatory and neoplastic lesions including benign and malignant categories. The frequencies of histological diagnosis were studied separately and also in combination with age group.

Results: The prevalence of cervical biopsies as regards to the total biopsies was studied and found to be 14%. The predominant pathology was nonspecific inflammatory lesions (79%). Among the precancerous and invasive lesions, most common was squamous cell carcinoma (14.7%).

Conclusion: This study revealed the prevalence of various cervical lesions diagnosed in Dept of pathology, Cuttack.

Key words: Cervical lesions, histopathology, squamous cell carcinoma

Introduction

The cervix is both a sentinel for potentially serious upper genital tract infections and a target for viral and other carcinogenic agents, which may lead to invasive carcinoma. Inflammations constitute one of the most common clinical abnormality detected followed by cancer threat. Cervical cancer is one of the leading cancers in woman with an estimated 500,000 new cases every year, of which 80% occur in developing countries.

1. Biswal, P et al., 2013
India, it is estimated to be over 140,000 cases. However, cervical carcinoma is a preventable disease and a significant decrease in incidence and mortality can be expected with the effectiveness of the papanicolaou cytologic test in detecting cervical precancers.

Material & methods
The present study was carried for over a period of 4 years from Jan 2008 to Dec 2011. All cervical lesions reported from Department of Pathology were included in the study. (Table-1) Formalin fixed paraffin embedded blocks were routinely stained with heamatoxylin & eosin stain and studied by light microscope by the histopathologists. The reports from the previous registers were analysed, the age and clinical diagnosis were recorded and the incidence of different lesions was tabulated. Cases were divided into inflammatory and neoplastic categories comprising of benign and malignant types (Table-2).

Result
Cervical biopsies comprised 2575 (14%) of total biopsies (18459) in last 4 years. The inflammatory category comprising of non-specific cervicitis showed the highest incidence of 2059 (79%) cases. Only 6 (0.23) cases of tuberculous cervicitis were seen. Of the benign neoplasms, 48 (1.8%) cases were diagnosed as endocervical polyps, 24 (0.9%) cases as leiomyomatous polyps and 2 (0.07%) cases as microglandular endocervical hyperplasia. The Premalignant and malignant category of squamous origin observed were, 26 (1.24%) cases as low grade squamous intraepithelial lesion(LSIL), 6 (0.23) cases as high grade squamous intraepithelial lesion (HSIL), and 381 (14.7) cases as invasive squamous cell carcinoma. 03 (0.11%) cases of clear cell carcinoma were also reported.

Discussion
Chronic cervicitis, an extremely common condition in adult females, as also seen in our study is of importance as it may lead to endometritis, salpingitis and pelvic inflammatory disease through ascending spread. Tuberculous cervicitis is extremely rare and so also was evident in our study. Endocervical polyps represent the growth of redundant folds of endocervical mucosa, including both stroma and epithelium. Most of the cases were observed in middle aged women in our study. Very few cases (24 or 0.9%) of leiomyomatous polyps were also seen. Microglandular hyperplasia of the endocervical epithelium occurs in women taking oral contraceptives. Microscopically, a complex architecture comprising a mixture of small endocervical cells and reserve cells simulates carcinoma. Only 0.7% cases have been observed in present study.
After several decades as the most common gynecologic cancer, cervical carcinoma is now showing a significant decrease in incidence and mortality. Much credit for these dramatic gains goes to the effectiveness of the papanicolaou cytologic test in detecting cervical precancerous lesions. Cervical precancers have been classified previously on the basis of morphology as dysplasia and carcinoma in situ. Subsequently, the Bethesda system considered the intraepithelial lesions as a single disease process and termed cervical intraepithelial neoplasia (CIN) which was graded from I to III. Recently, the national cancer institute has proposed a new diagnostic terminology for cervicovaginal cytopathology deposits and reduced the three-grade CIN scheme to two grades of squamous intraepithelial lesion (SIL). The lesions formerly designated as CIN I, would be termed low grade squamous intraepithelial lesion, (LSIL) whereas those lesions previously called CIN II & CIN III would be encompassed under the designation of high grade squamous intraepithelial lesion, HSIL. The valid reason for use of new terminology is the differential distribution of HPVs. HPV 6 are associated with flat and exophytic condylomas and HPV 16 and 18 are found in CIN III and invasive carcinomas.

Invasive squamous cell carcinoma was observed in 381 cases (14.7%), majority being noted in 4th (112 cases) and 5th (156 cases) decades. They are classified into 3 grades like large cell keratinising (well differentiated), large cell non-keratinising (moderately differentiated) and small cell non-keratinising (poorly differentiated). In concordance to literature, we also observed majority of these cases in large cell non-keratinising grade. Primary adenocarcinomas that make up 5% to 15% of all carcinomas of the cervix comprised of 0.58% in our study. Clear cell carcinoma of cervix that carries a good prognosis and usually observed in young females was also observed in our study. Mostly hysterectomy specimens without any pathology in the cervix were also encountered in the study.

At the onset of menarchy, the production of estrogen by the ovary stimulates various changes in the cervical mucosa resulting in some degree of cervical inflammation resulting in virtually all multiparous and in many nulliparous adult women. However, chronic non-specific cervicitis is usually of little clinical consequence, specific infection by gonococci, clamydiae, mycoplasma and herpes simplex virus (type-2) are significant as regards to upper genital tract disease, pregnancy complication, or sexual transmission. In
our study the incidence of chronic cervicitis is 79%.

Endocervical polyps are relatively innocuous inflammatory tumours that are only significant for their production of irregular vaginal “spotting” of bleeding that arouses suspicion of some more ominous lesion. The occurrence of polyps is found in 2 to 5% of adult women and in our case it was 2.7%.

References

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<tr>
<th>Year</th>
<th>Total no of biopsies</th>
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<td>3619</td>
<td>566</td>
</tr>
<tr>
<td>Jan 2009 - Dec 2009</td>
<td>4762</td>
<td>608</td>
</tr>
<tr>
<td>Jan 2010 - Dec 2010</td>
<td>4874</td>
<td>627</td>
</tr>
<tr>
<td>Jan 2011 –Dec 2011</td>
<td>5204</td>
<td>774</td>
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<td><strong>Total</strong></td>
<td><strong>18459</strong></td>
<td><strong>2575</strong></td>
</tr>
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</table>
### TABLE-2

The frequency of histological diagnosis of cervical lesions separately and in combination with age group.

<table>
<thead>
<tr>
<th></th>
<th>1-10 Years</th>
<th>11-20 Years</th>
<th>21-30 Years</th>
<th>31-40 Years</th>
<th>41-50 Years</th>
<th>51-60 Years</th>
<th>61-70 Years</th>
<th>71-80 Years</th>
<th>Total</th>
<th>%</th>
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<tr>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic cervicis</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>0.23</td>
</tr>
<tr>
<td>Tuberculous cerv</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Benign</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocervical polyp</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>3</td>
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<td>48</td>
<td></td>
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<tr>
<td>Leiomyomatous polyp</td>
<td>-</td>
<td>1</td>
<td>9</td>
<td>8</td>
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<td>2</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Endocervical hyperplasia</td>
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<td>-</td>
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<td>2</td>
<td>9</td>
<td>5</td>
<td>8</td>
<td>1</td>
<td>1</td>
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<td>25</td>
<td>1.26</td>
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<td>1</td>
<td>3</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HSIL</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Invasive SCC</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>112</td>
<td>156</td>
<td>59</td>
<td>33</td>
<td>18</td>
<td>381</td>
<td>14.7</td>
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<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
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<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>0.11</td>
</tr>
</tbody>
</table>
Cancer cervix is the second most common cancer in females with a very high mortality rate. Pap smear study remains gold standard test for screening, detection and follow up of cervical cancer. The aim of our study was to evaluate the number of pap smears studied during 2011 at AHRCC, as per their age, clinical presentation and microscopic findings. Out of 1470 pap smears studied in the year 2011, maximum number of cases were in the 4th (31.83%) and 5th (32.78%) decades of life. Inflammatory smears were more common (54.76%). Squamous cell carcinoma found in 34.28% cases, 7.61% were suspicious/HSIL smears and radiation changes were observed in 1.90% cases. Only 1.42% cases were haemorrhagic/inadequate out of 502 post treatment (post op. & post RT) follow up cases 104 (20%) showed recurrence and 28 (5.57%) showed radiation changes and rest did not show any evidence of disease. Pap smear is the most successful test in diagnosing cervical cancer. It has been decided internationally that every women above 30 year age must have at least one pap smear examination per year. It is also of gold standard for post treatment follow up to rule out or confirm recurrence of disease.

Key words: cancer cervix, pap smear.

Introduction
Worldwide, malignant lesions of the cervix represents the most frequent cause of mortality and morbidity among women in developing countries. Its the third most common cause of cancer death in females.1 Every year more than one million women in the world suffer from this cancer and more than 2.5 lakh deaths over per year. In India more than 1,00,000 new cases of cancer cervix reported per year.2 Its the most frequent neoplasm constituting 20%-50% of all neoplasms in India.3,4 In general, higher incidence of cancer cervix are found in developing
countries contributing 83% of reported cases annually where as developed countries add only 3.6% of new cases.\textsuperscript{5} Although prevention and early detection are established to be highly effective in controlling cervical cancer, lack of awareness in many developing countries is the main barrier in its way. Pap smear

**Abstract**

Cancer cervix is the second most common cancer in females with a very high mortality rate. Pap smear study remains gold standard test for screening, detection and follow up of cervical cancer. The aim of our study was to evaluate the number of pap smears studied during 2011 at AHRCC, as per their age, clinical presentation and microscopic findings. Out of 1470 pap smears studied in the year 2011, maximum number of cases were in the 4th (31.83\%) and 5th (32.78\%) decades of life. Inflammatory smears were more common (54.76\%). Squamous cell carcinoma found in 34.28\% cases, 7.61\% were suspicious/HSIL smears and radiation changes were observed in 1.90\% cases. Only 1.42\% cases were haemorrhagic/inadequate out of 502 post treatment (post op. & post RT) follow up cases 104 (20\%) showed recurrence and 28 (5.57\%) showed radiation changes and rest did not show any evidence of disease. Pap smear is the most successful test in diagnosing cervical cancer. It has been decided internationally that every women above 30 year age must have at least one pap smear examination per year. It is also of gold standard for post treatment follow up to rule out or confirm recurrence of disease.

Key words : cancer cervix, pap smear.

**Introduction**

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cervix. It was introduced in 1943 by George Papanicolaou, after whom it is named. The test is simple, quick, of low cost and less painful. It has been estimated that the use of this simple and cost effective technique has reduced the incidence of cervical cancer by 79% and mortality by 70%. Unfortunately many developing countries lack the awareness and facility to carry out widespread pap screening.6,7

Material and methods
Cervical smears collected in the Gynaec Department during Jan-Dec 2011 were received in the Dept. of Oncopathology, AHRCC and pap stain was done. Age and clinical details of patients were recorded. The slides were examined by the cytopathologist and the results were recorded. Analysis of observations were made and compared with age, clinical details.

Results
Out of 1470 pap smears studied in the year 2011, maximum number of cases were in the 4th (31.83%) and 5th (32.78%) decades of life. Inflammatory smears were seen in 805 (54.76%) cases, 504 (34.28%) cases were squamous cell carcinoma, 112 (7.61%) were suspicious/HSIL cases and radiation changes were observed in 28 (1.90%) cases. Only 21 (1.42%) were inadequate or haemorrhagic smears. Out of 502 post treatment (post op and post RT). Follow up cases 104 (20%) showed recurrence and 28 (5.57%) cases showed radiation changes and rest did not show any evidence of disease.

Discussion
Cervical cancer is the most common gynaecologic cancer in women and in the leading cause of cancer death in women in under developed countries. Pap smear has been the gold standard screening test for cervical cancer since its introduction in 1949. It has helped reducing the cervical cancer mortality rates roughly to half.8 There are various risk factors responsible for the development of cancer cervix, they are sexual factors like early pregnancy, multiple sexual partners etc. multiparity, smoking, OCP, low socioeconomic status, and viral infection, most commonly Human Papilloma Virus. On the basis of microscopic findings carcinoma cervix is broadly divided into squamous cell carcinoma and its variants (most common cancer of cervix), adenocarcinoma and its variants, both of them constitute around 99% of all cervical cancers.

The 2001 bethesda system for reporting of pap smear classifies squamous cell abnormalities into four categories (I) ASC (Atypical squamous cells: with two sub categories : “ASC-US” (Atypical
squamous cells of undetermined significance) and ASC-H (atypical squamous cell can not exclude HSIL), (II) LSIL (low grade squamous epithelial lesion), (III) HSIL and (IV) squamous cell carcinoma ASC-US is defined as cytologic changes that are insufficient for diagnosis of LSIL, whereas ASCH refers to cytologic changes that can not exclude diagnosis of HSIL. As these terms reflect inability of a cytopathologist to give definite diagnosis of LSIL of HSIL in a particular case, percentage of such cases should be restricted.

Carcinoma cervix is preceded by a prolonged premalignant phase. Therefore, determination of stage of the disease process is very essential for proper clinical management. Pap smear study is also useful for post OP/Post RT follow up to rule out recurrence or persistence of the disease.

References
### Table 1
Age distribution of cases

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<td>Nil</td>
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<tr>
<td>21 - 30</td>
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<td>31 - 40</td>
<td>218</td>
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<td>41 - 50</td>
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<td>51 - 60</td>
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<tr>
<td>81 - 90</td>
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<tr>
<td>91 - 100</td>
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### Table 2
Distribution of cases as per Microscopic Findings

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<th>Microscopic Findings</th>
<th>No. of cases</th>
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<td>54.76</td>
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<td>2.</td>
<td>Squamous Cell Carcinoma</td>
<td>504</td>
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<td>3.</td>
<td>HSIL</td>
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<td>7.61</td>
</tr>
<tr>
<td>4.</td>
<td>Radiation Change</td>
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<td>5.</td>
<td>Inadequate</td>
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<td><strong>Total</strong></td>
<td></td>
<td><strong>1470</strong></td>
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### Table 3
Correlation between clinical diagnosis and microscopic findings

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<tr>
<th>Clinical Diagnosis</th>
<th>No. of cases</th>
<th>Inflammatory</th>
<th>Squamous Carcinoma</th>
<th>HSIL</th>
<th>Inadequate</th>
<th>Radiation Changes</th>
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<tbody>
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<td>Ca Cervix</td>
<td>695</td>
<td>270</td>
<td>335</td>
<td>82</td>
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<td>354</td>
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<td>28</td>
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<td>Post Op/RT</td>
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<td>60</td>
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<td>01</td>
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<tr>
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<tr>
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Introduction
Cervical Cancer continues to be an important public health problem affecting women’s health in developing world. 80% of estimated annual global burden of 500,000 new cases and 280,000 deaths occur in developing countries due to lack of effective screening programme. It is the most frequent neoplasm in India contributing 20-50% of all neoplasm. Every year more than 1,00,000 new cases of this cancer are reported in India. Early detection and treatment of precancerous lesion can prevent progression to Invasive cervical cancer. Out of various methods available for early detection Cytology, Colposcopy and Histopathological study are being used most commonly all over the world. Cytology still remains to be most practical, effective and fairly sensitive procedure for the diagnosis of the disease but on the other hand it cannot delineate about the site, location or the extent of the disease process. Colposcopy is a technique meant primarily to assist the physician in the examination of the visible portion of the genital tract and hence complements Cytology. Colposcopy has produced a new outlook in the understanding of cervical diseases. The ability of Colposcope to outline the lesion, to study its qualitative changes and to observe in a dimension other than vertical one of histology is invaluable. It can determine the site and extent of the disease process and also preclinical cervical cancer which would have been missed by a Cytosmear. It has solved the problems in determining and stipulating the type of biopsy techniques without which a random biopsy may well miss the very spot. Histopathology is the ultimate technique for giving the final
diagnosis about the presence of atypical cervical lesions including basal cell hyperactivity, CIN or micro invasive Carcinoma. Colposcopy stands between Cytology and histology i.e Population Screening and definite tissue diagnosis. Keeping all these in view, the study of Pap smear, Colposcopy and directed biopsy were carried out on Unhealthy cervix to find out the prevalence of precancerous and cancerous lesion in western part of odisha. Furthermore, attempt has been made to correlate the findings of these procedures to assess the accuracy of each method for early detection of cervical neoplasm.

**Methods**

The study was undertaken in the Dept of O & G, VSS Medical College, Burla for a duration of 2 years from December 2003 to December 2005. Total no 202 cases were clinically screened with relevant complaints and subjected for Cytological & Colpscopic evaluation to detect suspicious lesions of neoplasia. 15 such suspicious cases were subjected to Colposcopic directed biopsy.

**Results**

The final diagnosis based on histology revealed that the incidence of CIN I, CIN II, III and Invasive cancers were 1.98 %, 1.48%, 1.48% and 1.98 % respectively. Majority of patients were from age group of 31 to 40 yrs. Most of the neoplastic lesions were found in grand multipare and multipare. The incidence of neoplastic lesions increase with parity. Most of the patients (67.8%) were from lower socioeconomic status. Although Metrorrhagia was the commonest complaint in the study group, patients with post menopausal and post coital bleeding were at maximum risk of developing cervical intraepithelial neoplasia. While maximum no of invasive carcinoma had gross appearance of growth in cervix, maximum no CIN changes were having cervical erosion.

Cytology revealed Chronic Cervicitis (24.75%) as most common finding where as neoplastic changes found in 6.4% of the study group. Trichomoniasis was the most common infection (19.8%). Colposcopy revealed maximum no cases are inflammatory (35% ) . The incidence of colpo-suspicious neoplasia was 7.45%.

While cyto-histological correlation was 90% for CIN, Colpo-histological correlation was 91%. Both cyto-histological and colpo-histologica correlation was 100% for invasive carcinoma. While Pap smear was nearly 92% Sensitive, colposcopy was nearly 98% sensitive to detect cervical neoplasia.

**Conclusion**

The easy accessibility of the cervix to Inspection, Palpation and application of Cytology in tissue sampling have led to
extensive screening programme for early detection and treatment resulting significant lowering of mortality from carcinoma cervix. Colposcopy is of outmost concern for a gynaecologist as it pinpoints the most suspicious area for directed biopsy to know the exact nature of the lesion, which is of much value to plan out the proper line of management. Cervical Cytology on the other hand though comparatively less accurate is a wonderful procedure at its own place. It is quite efficient to pinpoint the suspicious group in which further evaluation can be done. Its place in mass screening programme is unquestionable. The overall accuracy improves maximum if cytology and Colposcopy are simultaneously combined. It is well told that “Pap smear discovers the crime and Colposcope locates the culprit”. Colposcopy directed biopsy yields the final verdict, which unmasks the true nature of the cervical lesion. So all the patients with symptoms and signs of unhealthy cervix should be routinely evaluated with Cytology and Colposcopy to ensure the optimal detection and directed biopsy for final diagnosis in suspicious cases. With all these modalities if properly implemented in place with determination, time is not far away when cervical cancer will be left behind as a disease of historical importance.

References
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Introduction

Cervical cancer is the fifth most common cancer in humans, the second most common cancer in women worldwide and the most common cancer cause of death in the developing countries. Sexually transmitted human papilloma virus (HPV) infection is the most important risk factor for cervical intraepithelial neoplasia and invasive cervical cancer (1). The worldwide incidence of cervical cancer is approximately 510,000 new cases annually, with approximately 288,000 deaths worldwide (2). Unlike many other cancers, cervical cancer occurs early and strikes at the productive period of a woman’s life. The incidence rises in 30-34 years of age and peaks at 55-65 years, with a median age of 38 years (age 21-67 years)(3). Estimates suggest that more than 80% of the sexually active women acquire genital HPV by 50 years of age (3). Cervical Cancer is a significant public health concern in India, with an estimated 134,420 incident cases and 72,825 associated mortalities in 2008. Compared to women in United States, women in India are five times more likely to develop and seven times more likely to die from Cervical Cancer (4). In 2008, there were an estimated 530,000 incident cases and 275,000 associated mortalities (4). Current data suggest that of the total burden, 86 percent of all cervical cancer diagnoses and 88 percent of associated mortalities occur among women living in economically developing regions of the world (4, 5). In addition, to significant disparities in the actual incidence of Cervical Cancer between countries, substantial differences in the overall contribution of Cervical Cancer to total Cancer burden also exist. In many economically developing countries, Cervical Cancer represents 13 percent of all female cancers compared to less than...
six percent in other regions of the world(4).

In light of India’s rapidly growing and aging population, the overall burden of incidence and mortality of Cervical Cancer in India is projected to increase by 68 and 78 percent, increase from 78,825 in 2008 to 129,792 by the year 2030(4). The prevalence and burden of Cervical Cancer is much higher among women of low SES, as well as among rural women of India (6). The level of sexual activity of a person will affect the risk of acquiring HPV infection. Early age of first intercourse, multiple sexual partners, unprotected sex and sex with uncircumcised men, have been found to increase the risk of contracting HPV infection (7). There are additional factors that increase the risk of developing Cervical Cancer after contracting HPV infection. These include smoking, oral contraceptive use, high parity, and infection with other sexually transmitted diseases such as HIV, Herpes, Chlamydia, Gonorrhea and Syphilis (8).

The aim of the study we performed at AHRCC was to evaluate the epidemiological and clinical aspects based on Gynecological and Obstetrics history of patients.

**Methods**

In this retrospective study, we have studied the records of 82 patients at AHRCC, Cuttack from January to June, 2012 and analyzed the data regarding different epidemiological factors associated with cancer cervix.

**Results**

Mean age at presentation is 54.96 years, age ranging between 27-82 years. Most of the patients were Hindus (96.3%), while the rest were Muslims (3.65%). Bleeding per vagina (63%), excessive foul smelling discharge per vagina (50%), post coital bleeding (3.65%) and irregular Vaginal Bleeding (6.09%) were the predominant symptoms. Average age at Menarche is 13.51 (12-16) years; average age at marriage is 16.81 (12-23) years; average age at first child birth is 18.67 (15-26) years and average age at menopause is 41.5 (32-59) years.

All the cases had cytological and histological confirmation of the disease. The clinical extent of the disease was classified according to FIGO system. Only 1 (1.21%) was found in Ca Cx IA, 12 (14.63%) was found in IB, 3 (3.65%) in IIA, 19 (23.17%) in IIB, 5 (6.09%) in IIIA, 34 (41.46%) in IIIB and 1 (1.21%) in Ca Cx IV. Out of 82 cases, 71 (86.58%) of women were diagnosed as squamous cell carcinoma, 4 (4.87%) as adenocarcinoma, 1 (1.21%) as adenosquamous cell carcinoma and 6 (7.31%) as inflammatory smears.

They were preferentially housewives, began early sexual life, and had greater
number of pregnancies and number of deliveries (parity from 1 to 12) and only 10 (12.9%) faced miscarriage. 56 (68.29%) consumed one or the other forms of tobacco.
70.73% were found in lower class, 23.17% were found in Middle Class and 3.65% were found in High class.

Discussion
Mean age of presentation is 54.96 years which shows that there is lack of awareness of Cervical Cancer among the patients, while mean age of presentation in Kerala was found to be 34.5 ± 9.23 years. (10)
A low incidence of Cancer of Cervix has been reported in countries where population is predominantly Muslim (Tomatis et al., 1990) (9) and the same was reflected in our study (3.65%). Besides, male circumcision can protect women against STD’s like HIV can also be put forth (Dr. Bertran Auvert et al., 2005).
Average age at menarche is 13.51 years in our study; a study in Lucknow (11) also shows mean age of Menarche to be 12.84±1.4 years which resembles my study.
Average age at marriage is 16.81 years whereas WHO report (12) suggests that average age of marriage is 22.2 years for Indian women. An explanation to this can be owed to child marriage is more popular in the rural classes of Odisha and the least age of marriage is as early as 12 years.
Average age at first child birth is 18.67 years whereas in Mexico, mean age at first child birth is 21.3 years and New Zealand it is 30.5 years (13). This too, is the consequences of early child marriage and onset of early sexual life in the rural population.
Average age at Menopause is 41.5 years while average age of menopause in India is 47.5 years, according to “The Indian Menopause Society’s 2008 Consensus statement.” Since, it’s a hospital based data on a minimal number of subjects, so this accounts for the fall in average age at menopause. Besides, many environmental and genetic causes can be the reason behind the fall in menopausal age.
Parity of more than three is observed in 83.33% of my population, thus multiparity is one of the risk factor for Cervical Cancer, especially among HPV positive women (Eluf Neto et al., 1994), can also be said.(14)
Besides consumption of one or more than one variety of smokeless tobacco and chewing tobacco is found in majority of subjects, this is also a risk factor for Cervical Cancer, which also correlates with the study done on Sudan women (Alkhair Abd Almahmoud Idris et al., 2010) (15).
A previous study mentioned that carcinoma of the uterine cervix primarily affects women from the lower socioeconomic class and those with poor access to routine medical care which correlates with my study (16).

References


Cancer is a biologic continuum and a dynamic process which is artificially compartmentalized by staging system. Staging system needs to be evidence based and user friendly. It is ever changing, depending upon development of acquisition of new knowledge.

**Stage** - Classification of cervical cancer according to the extent of the growth was first published in 1929 by the Cancer commission of Health Organization. Later when FIGO (International Federation of Gynecology and Obstetrics), founded in 1957, adopted this classification in 1958. There after the staging of cervical cancer became known as FIGO staging system. Neither the TNM System (developed by Pierre Denoix between 1943 and 1952 and first published in 1953) nor AJCC staging system (published in 1977) had much influence on FIGO staging of cervical cancer. FIGO staging was based on anatomical compartmental spread of cervical cancer. This was necessary. It helped in evaluation of surgical resectibility in each patient. Even if the surgical resection was not deemed satisfactory, surgical findings and subsequent accurate anatomical pathology findings could be used to prescribe tailored adjuvant therapies.

Over the years- except that of cervical cancer which is staged clinically, all other Gynecological Cancers are staged surgico-pathologically. The purpose of clinical stage is to select & evaluate therapy, whereas, pathological stage does provide the most precise data to estimate prognosis & calculate end result.

**Purpose of staging:**
- To offer a classification of a cancer’s extent.
- To provide a uniformly comparable optimal treatment modality without confusion or ambiguity.
• To formulate a prognosis of the patient.
• To help disseminate knowledge by providing common international language.
• To facilitate clinical research, producing new data on similar group of patients, integrating them.
• Staging is a means of communicating between one institution to another.
• Is a means of evaluating the treatment plans used within one institution.
• Method of staging should remain fairly constant.
• Staging does not limit treatment plan, therapy is tailored to the individual need.

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**Principle of staging**

Stage I - Early stage disease-lesion is confined to the organ of origin.

Stage II - Disease extension beyond the site of origin to involve adjacent organs or structures.

Stage III - More extensive involvement.

Stage IV - Represents metastatic disease

Basic stages are then sub staged, which are usually a reflection of specific prognostic factors within a given stage

**Staging of cancer cervix-**

A. FIGO staging- clinical staging

B. TNM staging

**Staging Procedure-**

FIGO-Clinical staging

**Extended clinical staging**

**Surgical staging**

A. FIGO staging-Clinical Staging

**Rationality of clinical staging**- Cervical cancer is primarily a local disease in pelvis, mostly detected in advanced stage in developing world, where this disease is abundant. Surgical staging system cannot be uniformly employed because of following reasons;

i. Affordability

ii. Surgical staging expertise

Surgical staging should be confined to investigational settings as there is no definite proven benefit as on today.

Cervical cancer is a clinically staged disease. FIGO staging system is the standard and is applicable to all histologic type of cervical cancer. FIGO does not include CT and MRI in staging procedure, rather encourages the use of diagnostic imaging techniques for evaluation of size and extent of lesion(s), whenever such facilities are available.

• Physical examination
• Palpate Lymph nodes
• Examine vagina and external genitalia
• Bimanual rectovaginal examination preferably under anaesthesia by experienced hand
• Radiological studies
• IVP, Barium enema- not mandatory (Enlarged committee-Jan-2009)
• Chest and skeletal x-ray- if indicated as metastatic work -up

• Procedures
• Biopsy
• Conisation- indicated In
• Positive ECC
• Unsatisfactory colposcopy
• Persistent CIN-1 (usually > 1 year), CIN-2, CIN-3 or CIS
• Diagnosis of microinvasive lesion is made on punch or wedge biopsy
• Discrepancy in cytologic, colposcopic, or pathologic finding.
• Endocervical curettage
• Colposcopy indicated in
• Abnormal appearing cervix
• Persistent post-coital bleeding or discharge
• Persistent CIN-1,2,3 on cytology
• ASCUS smear with positive high-risk HPV testing
• Hysteroscopy

Cystoscopy/Proctoscopy/Proctosigmoidoscopy
• Should be performed with symptoms consistent with presence of fistula of urinary bladder or lower GI tract
• Advanced stage disease
• Optional studies- FIGO does not allow to change clinical stage by Information gathered from such studies.
• CT scan / MRI/PET scan
• Ultrasound
• Laparoscopy
• Venography
• Arteriography
• Lymphangiography
• Radio nucleotide scanning
• Laparoscopy
• FNAC of suspicious nodes.
• Pathologists findings on the post operative HPE
• Staging must not be changed after subsequent findings by either extended clinical staging or surgical staging
• When there is doubt. The earlier stage is allocated

Limitation of clinical staging-
Discrepancies of up to 25% in early stage and 65-90% in advanced stage (e”IIIB), between clinical and surgical staging have been reported2.
• There may be inaccuracy and inter-observer difference in assessing the parametrium
• Little information available about UV and RV space
• Estimation of tumour size, more so when growth is endocervical
• Extension in to uterine cavity, which is a poor prognostic factor, cannot be assessed
• Lymphnode metastasis cannot be evaluated

Extended clinical staging
It is desirable to estimate tumour volume and the presence of lymph node metastases before surgery so that the treatment plan for node positive and high risk node negative patients could be changed to
chemo-radiation alone, avoiding the potential high rate of complications associated with a combination of radical surgery and postoperative radiotherapy. CT scan, MRI, PET, lymphangiography and laparoscopy have been used to improve staging of cancer cervix. These are usually useful in assessment of parametrial extension and lymphnode metastasis (CT, MRI, and PET). A combined use of MRI and PET for pre-treatment staging of inoperable (Ib2 and stage II A2 & B to IVa) cervical cancer has led to a better understanding of the relationship between FIGO stage, tumour volume, tumour infiltration and nodal metastases. Systematic review comparing CT scan with MRI showed that MRI is significantly more sensitive with equivalent specificity. MRI has excellent sensitivity for the detection of parametrial diseases. So MRI is the preferred study to evaluate tumour size, lymphnode metastasis, and local tumour extension. MR imaging is most commonly performed in patients being considered for fertility-sparing radical trachelectomy. Positron emission tomography (PET) has been reported to have sensitivity and specificity of 100% and 99%, respectively. PET is still under evaluation, and is compared with surgical nodal staging.

Because these modalities of tests are not available equally throughout the world and the interpretation of the results can be variable, these studies are not recommended by FIGO for staging purpose. They may be useful in individual treatment planning and be recorded for future guidance.

**Surgical staging**

Surgical evaluation, although not practical or feasible in all patients, can more accurately identify metastatic disease. It is advocated by some who believe that surgical information details the extent of disease, allowing the treatment to be tailored to the individual, whereas some believe this method to be used only in clinical trial settings. However, surgical evaluation of retroperitoneal lymphnodes offers accurate description of pelvic and paraaortic lymphnodes. Dissection of common iliac and paraaortic region and macroscopic lymphnode is recommended. By surgical staging, debulking of gross positive node(s) is possible with improved survival and modification of radiation field and chemotherapy can be planned for
optimal treatment. It is true that surgical staging, (subjective variation in node sampling not withstanding) did provide better prognostic information then clinical staging. Surgical staging is associated with increased treatment related morbidity.

Pretreatment evaluation of pelvic and paraaortic lymphnodes

- **Procedure**
  - Laparotomy
    - Not advisable
    - It adds to morbidity
  - Laparoscopy
    - Sampling of lymphnodes
    - With CT +ve nodes in early stage
    - Negative nodes in extensive lesion

Advantage of surgical staging

- Identification of clinically occult extrapelvic disease sites
- Excision of inflamed adnexae, which may complicate radiotherapy
- Down staging of patients to allow for more appropriate treatment

Place – not agreed upon by FIGO

- It is beneficial for radiotherapy
- It cannot be employed world wide
- Expensive, delays treatment, increases complication from adjuvant radiation

**It can be employed in clinical trial or research protocol**

Non surgical staging is still the gold standard for advanced cervical cancer treatment planning unless well designed phase III study could show a significant survival benefit of surgical staging. The roles of molecular imaging (new MRI technology or PET with FDG or other radiotracers) as an early predictor of response to treatment need more researches.

### A. TNM classification (Tumour, Node, Metastasis)

- is proposed by American Joint committee Commission on cancer and is mainly used in documenting findings on surgical and pathologic evaluations as the pathologic stage of the disease. If there is ambiguity regarding the correct stage, the lower stage is assigned.

<table>
<thead>
<tr>
<th>FIGO</th>
<th>AJCC</th>
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<td>Stage 0</td>
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<tr>
<td>IA1</td>
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**The following table shows the FIGO and AJCC Stage Grouping:**

**Rules for Classification:**

- FIGO GUIDELINES-2000
- Stage 0- Full-thickness involvement of epithelium – no sign of invasion in to stroma
- Stage IA1 & A2- based on microscopic exam., preferably cone biopsy specimen- depth of invasion should not be >5mm and horizontal spread not >7mm
- LVSI should not alter staging- specially mentioned
- Larger lesions (>5mm, >7mm) should be staged as Stage IB
- Extension to corpus is disregarded- as it is impossible to estimate it clinically.
- Hydronephrosis/ non-functioning kidney- Stage III
- Bullous oedema- no importance, Ridges and furrows into bladder wall- sub mucous involvement. +ve cytology of washing of UB requires HP confirmation to stage as IV

**Revised FIGO Staging of carcinoma of Cervix-2009**

The following changes were made from that of 1994. The author had the opportunity to play a small role during revised staging procedure which was initiated from 2006.

1. Deletion of stage-o
2. Stage IIA – subdivided in to IIA1(d”4cm) and IIA2(>4cm)

**Stage-I** - Cervical carcinoma confined to uterus (extension to corpus should be disregarded)

**Stage-IA** - Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions- even with superficial invasion are Stage IB

**Stage-IA1** - Stromal invasion not greater than 3mm in depth and 7mm or less in horizontal spread

**Stage-IA2** - Stromal invasion >3mm, not more than 5mm with horizontal spread 7mm or less

**Stage-IB** - Clinically visible lesion confined to cervix or microscopic lesion greater than IA2

**Stage-IB1** - Clinically visible lesion 4cm or less in greatest dimension

**Stage-IB2** - Clinically visible lesion >4cm in greatest dimension

**Stage-II** - Tumour invades beyond the uterus but not to pelvic wall or to lower third of the vagina

- **Stage-IIA** - Without parametrial invasion
  - **Stage-IIA1** - Lesion <4cm
  - **Stage-IIA2** - Lesion >4cm

**Stage-IIIB** - With parametrial invasion

**Stage-III** - Tumour extends to pelvic wall and/ or involves lower third of vagina and / or causes hydronephrosis or non-functioning kidney

**Stage-III A** - Tumour involves lower third of vagina, no extension to Pelvic wall

**Stage-III B** - Tumour extends to pelvic wall and/ or causes hydronephrosis or non-functioning kidney

**Stage-IV** - The carcinoma gas extended beyond the true pelvis or has clinically involved the mucosa of the bladder or rectum. A bullous oedema, as such does
not permit a case to be allotted to stage IV

**Stage-IVA-** Tumour invades mucosa of bladder or rectum and/ or extends beyond true pelvis

**Stage-IVB-** Distant metastasis

**Conclusion-** Carcinoma cervix remains a clinically staged disease, though it cannot accurately access tumour extension or lymphatic involvement. Staging is improved by radiological tools like CT, MRI, and PET. MRI is more useful in assessment of parametrial involvement, whereas, CT, MRI, and PET are complementary to each other in assessing lymphnode involvement. These imaging modalities, though not mandatory, can be used when facilities are available for better management.

**Reference :**


Abstract

Introduction:
In medical science Cervices from hysterectomies and biopsies constitute the majority of gynaecological specimens which are received in the department of histopathology and non-neoplastic lesions form the huge chunk of diagnosis among them. However, there are many lesions that appear to be exuberant and can be misdiagnosed to be malignant and vice versa. On the basis of this, a detailed histomorphological analysis of the non-neoplastic and neoplastic lesions of the cervix was taken up. The purpose of this study is to determine the frequency and morphological patterns of non-neoplastic and neoplastic cervical lesions at S.C.B. Medical College, Cuttack during the period from January 2012 till December, 2012.

Material and Methods: All the cervical lesions either from hysterectomy or biopsy specimens received and diagnosed in Dept. of Pathology, S.C.B. Medical College, Cuttack during a period of one year from January 2012 till December 2012 were analysed. These cervices were subjected to detailed gross and microscopic examination and were further subclassified into various non-neoplastic and neoplastic categories. The frequency and spectrum of different histopathological diagnoses were evaluated according to age group and clinical diagnosis.

Results: Out of the total 4669 histopathological samples received in 2012, cervical lesions comprised 14.28% or 667 cases. The non-neoplastic lesions were majority accounting for 636 (95.4%) cases inclusive of 624 or 93.5% cases of chronic non-specific cervicitis. Out of
malignant lesions, squamous cell carcinoma was the most common and predominantly of well differentiated (Large cell keratinising) type.

**Conclusion:** During the study, a number of non-neoplastic lesions of the cervix were encountered, which caused a great deal of morbidity to the patients. It has been recommended to take up further community based studies in association with a microbiological and colposcopic correlation to evaluate the exact incidence of these non-neoplastic lesions of the cervix. Many of the neoplastic and precancerous lesions are also discovered accidentally which therefore mandates a routine histopathological examination of all cervices removed from patients for any cause.

**Key words:** Cervical lesions, Histopathology, LSIL, SCC

**Introduction:** Gynaecological specimens form the substantial proportion of the workload in most of the histopathological departments.¹ In the female genital tract, the uterine cervix is a gateway to several non-neoplastic and neoplastic gynecological lesions.² Most of these lesions are commonly found in women of reproductive and postmenopausal age. These lesions constitute a major source of morbidity and mortality in women worldwide. Hence the need to analyze them to provide a baseline data of the pattern of these lesions in our local environment.

The present study was undertaken with the following aims and objectives:

- To study the various gross and microscopic features of the uterine cervix in non-neoplastic and neoplastic lesions.
- To categorize these lesions into different groups.

**Material & methods:** All uterine cervical biopsies received at the Department of Pathology, S.C.B. Medical College, Cuttack over a period of one year from January 2012 till December 20112 were the materials for this study. These specimens were sent from the Dept. of Obstetrics & Gynecology, S.C.B. Medical College, Cuttack and clinics and hospitals of other gynecologists. The biopsies were formalin fixed, routinely processed and paraffin blocks were prepared which were stained by H & E stain. The slides were evaluated by 3-4 histopathologists. These lesions are classified using the World Health Organization (W.H.O.) criteria³

The age and clinical diagnoses were recorded from the register and tabulated.

**Result:** Total number of samples received for histopathological examination in the Dept. of Pathology during the year 2012 was 4669. The cervical biopsies constituted 667 (14.28%) of total biopsies. Out of
these, non-neoplastic lesions were predominant accounting for 95.4% (636) of total cervical biopsies. From the non-neoplastic category, chronic non-specific cervicitis was the maximum comprising of 624 or 93.6% of cases (Table). The common age group for inflammatory lesions of cervix is 41-50 years (275 cases) followed by 31-40 years (161 cases) in frequency. The premalignant and malignant category included low grade squamous intraepithelial lesion (LSIL-1.9%), invasive squamous cell carcinoma (2.3%) and adenocarcinoma (0.4%) of uterine cervix. Squamous cell carcinoma is graded according to a three tier system (WHO) into large cell keratinising, large cell non-keratinising and small cell non-keratinising types. Out of 15 cases of squamous cell carcinoma, highest number of cases belonged to Grade I or large cell keratinising (Well differentiated) type and majority occurred in the age group 41-50 years. The common age group for adenocarcinoma was 51-60 years.

**Discussion:** Cancer of uterine cervix is an important cause of morbidity and mortality among women worldwide and a leading public health problem. It is the most common cause of cancer in women in developing countries and second most common cancer in women, worldwide. Early detection and treatment of precancerous lesions can prevent progression to invasive cervical cancer. Invasive squamous cell carcinoma of cervix is the end stage of a disease process beginning with atypical transformation of cervical epithelium at squamocolumnar junction leading to cervical intraepithelial neoplasia of advancing grades and eventually invasive carcinoma. Early detection and treatment of precancerous lesions can prevent progression to invasive cervical cancer. Many times therefore cervical biopsies are done to rule out presence of precancerous or invasive cervical lesions. Cervical biopsies in surgical pathology specimens comprise of either punch biopsy specimens or hysterectomy specimens where cervix is also examined. In order to find out the incidence of cervical lesions in the Dept. of Pathology, S.C.B. Medical College, Cuttack during the year 2012, this study was conducted where the age and clinical diagnosis along with histopathological findings were recorded from the register and tabulated and analysed.

Out of total 4669 surgical pathology specimens, cervical lesions accounted for 667 or 14.28% of cases. This finding is comparable to the observation of Biswal P et al who found out a total number of 2575 (14%) cervical lesions out of 18,459 biopsy specimens. This study was done
over a period of four years from 2008 till 2011 in the Dept. of Pathology, S.C.B.Medical College, Cuttack. Non neoplastic lesions of the cervix form a major bulk of the diagnosis among the gynaecological specimens, either the hysterectomy or the biopsy specimens. However, the reports are very non-specific, the commonest being “chronic cervicitis”. The term “chronic” in chronic cervicitis implies more on the duration of the symptoms rather than on the nature of the inflammatory cells in the cervical lesion. Therefore, a report of chronic cervicitis does not mean much to the clinician, as it becomes very difficult to correlate a clinical diagnosis. In the present study, we have got 93.5% (Table) of total cervical biopsies and 98% of non-neoplastic lesions as chronic cervicitis. This finding is comparable to that of Palipady A et al who got 100% of non-neoplastic lesions as chronic cervicitis.

Squamous metaplasia is a physiological change which is seen in the cervix through puberty, the reproductive years and menopause and hence, it is a very common finding on microscopy. An abrupt transition between immature and mature squamous metaplasia is known. It is important to recognize this entity histopathologically and hence avoid an over diagnosis of CIN. We got 12 cases (1.8%) of squamous metaplasia and all were mature squamous metaplasia seen in the age group 31-50 years..

In our series we got 13 cases (1.9%) of low grade squamous intraepithelial lesions (LSIL) but not a single case of high grade squamous intraepithelial lesions (HSIL). We have got only 31 cases of premalignant and malignant lesions of cervix in the present study which may be a small number to include all types of SILs. Koilocytic atypia caused due to human papillomavirus can be identified by detection of nuclear atypia, nucleomegaly and perinuclear clearing in the squamous cells and according to WHO these are included under the generic term LSIL. Patients 30 years of age and older have a higher risk of LSIL progression or persistence as compared to 20–29 year olds. In the above study majority of LSIL cases were detected after 30 years. So these cases should be followed up closely by the gynaecologists. Total number of cervical cancers encountered in our study are 18 out of total 667 cervical specimens which include 15 of squamous cell carcinoma and 3 adenocarcinoma cases.

It has been firmly established, both biologically and epidemiologically, that the main cause of cancer cervix is due to a persistent infection of high-risk human papillomavirus (HPV) types, which are
present in 99.7% of cancer cervix cases. Nevertheless, the presence of a persistent high-risk HPV infection risk is not sufficient to immortalize and transform the epithelial cells of the host; it has been confirmed that the presence of genetic and epigenetic alterations are needed for the development of carcinogenesis. As a result, these factors taken together may alter the control of the cell cycle, causing the host cell to acquire an immortal phenotype and ultimately progress towards a malignant and invasive phenotype.9

But due to prevalence of HPV infection in the pathogenesis of carcinoma cervix, HPV Vaccines have been in use for last few decades and aims at primary prevention of carcinoma of cervix. The vaccines available are Bivalent (Cervarix) and Quadrivalent (Gardasil) HPV vaccine Types. Indian Academy of Pediatrics (IAP) recommends that girls aged 10 to 12 years should be vaccinated. Vaccine can be administered up to the age of 26 years. Women remain at risk of infection throughout their sexually active lives and can therefore benefit from vaccination even up to the age of 45 years.10 Both the vaccines have demonstrated persistently high serum antibody levels and robust immune memories till 5-6 years after initial vaccination.

**Conclusion:**
During the course of this study, a number of non-neoplastic lesions of the cervix were encountered. These lesions were significant enough in their clinical presentations, as they caused a considerable amount of morbidity and loss of work hours, which was thus a financial burden.

Histopathology is considered as a gold standard in diagnosing the lesions of the cervix. However, there are many lesions that are mistakenly over diagnosed to be neoplastic. Therefore, it is recommended to take up further studies to evaluate these nonneoplastic lesions of the uterine cervix on a community basis.

Also, regular examination of cervix can diagnosed cervical lesions at pre-malignant or early malignant stage. Hence it can down stage cancer cervix.

**Reference:**
3. Siimionescu C, Margaritescu CL, Georgescu CV, Mogoanta L, Marinescu

<table>
<thead>
<tr>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of histological types of cervical lesions according to age group</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Chronic cervicitis</td>
</tr>
<tr>
<td>Metaplasia</td>
</tr>
<tr>
<td>LSIL</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Total</td>
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Abstract:
Cervical cancer is the fifth most common cancer in humans, the second most common cancer in women worldwide and the most common cause of cancer death in females in the developing countries. Since its introduction in 1949, pap smear has been the gold standard screening test for cervical cancer. The aim of our study was to analyse the number of pap smears studied during 2012 at the Department of Oncopathology, AHRCC, as per their age, clinical presentation and microscopic findings as well as to find out the incidence of carcinoma cervix and post operative and post-irradiation follow up of the cases.

Keywords: Cancer Cervix, Pap smear.

Introduction:
Carcinoma of cervix is a major global health problem and is the second most common cancer among women with an estimated 493,000 new cases and 274,000 deaths occurring annually all over the world. Current estimate indicates that every year about 5 lakh new cases of cancer cervix are diagnosed worldwide of which approximately 1.4 lakh cases occur in India. Now about 75,000 women die due to cervical cancer in India, but in developed countries like USA, UK the death rate is negligible. Recently WHO has classified carcinoma cervix as a preventable disease. Secondary prevention based on cervical screening has been successful in many developed countries. The widespread introduction of cervical screening by papanicolaou test, or pap smear has given dramatic result in reducing the incidence and mortality rate.
of cancer cervix in developed countries.\textsuperscript{2} Pap smears screening every 3-5 years with appropriate follow up can reduce cervical cancer incidence by up to 80\%.\textsuperscript{3} Unfortunately many developing countries lack the awareness and facility to carry out widespread pap screening.\textsuperscript{4,5}

**Material and Methods**
Cervical smears collected in the Gynaecological Oncology Department of AHRCC during Jan-Dec. 2012 were received in the Department of Oncopathology. AHRCC and pap staining was done. Age and clinical details of patients were recorded. The slides were examined and results were recorded. Analysis of observations were made and compared with age and clinical details.

**Results:**
Out of 1568 pap smears studied in the year 2012, maximum number of cases were in fifth decade of life. Inflammatory smears were most common found in 932 (54.43\%) cases 548 cases (34.94\%) were squamous cell carcinoma, 67 (4.27\%) cases were suspicious smears/HSIL cases and radiation changes were observed in 10 (0.6\%) cases only 11 cases (0.7\%) were inadequate on haemorrhagic smears.

Out of 387 post treatment (post op and post RT) follow up cases 53 showed recurrence, radiation change was found in 10 cases, 3 were inadequate smears and rest did not show any evidence of disease. Out of 751 cases clinically diagnosed as carcinoma cervix 493 were positive for carcinoma and 16 were HSIL cases. Out of 49 routine pap smear studied 3 cases showed HSIL change.

**Discussion:**
Carcinoma cervix is preceded by a prolonged Premalignant or non-invasive phase, (may range up to 20 years). During that period the premalignant or intraepithelial lesions shed abnormal cells. These cells can be detected by pap smear. This is of utmost importance which reduces the incidence of carcinoma cervix. Dr. George Nicholas Papanicolaou is said to be the father of Cytology since he could detect first cancer cells in the vaginal smears of cancer cervix patient in 1923. After long years of his dedicated hard work he published “new cancer diagnosis” in which the importance of pap smear test was mentioned in detail. Then the pap test was accepted and became a routine practice for screening and diagnosis and follow up in cancer cervix patients. Since its introduction in 1949, it has helped in reducing the cervical cancer mortality rates roughly to half.\textsuperscript{6}

There are various risk factors responsible for the development of cancer cervix. Out of which the most important cause
established now is human papilloma virus infection, along with other factors like early age at marriage, multiple sexual partners, multiparity and low socioeconomic status etc.7-8 Study conducted during 2010 and 2011 at AHRCC showed maximum number of patient turn over is within age range of 40-60 years.9,10 Our present study also correlates with it.

**Conclusion:**
For the reporting of pap smears, internationally The Bethesda System (2001) of reporting is followed, which includes specimen adequacy and nature of epithelial cell abnormality. It has been decided internationally that every women above the age of 30 years must have at least one pap smear examination to detect any epithelial cell abnormality. Pap smear is very useful in prevention, detection and in post treatment follow up of cancer cervix.

**References:**
9. S. Panda, S. Samantaray, N. Rout, S.K. Giri. Interpretation of Pap smear at AHRCC, Cuttack during


### Table 1

AGE DISTRIBUTION OF CASES

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of cases</th>
</tr>
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<tr>
<td>10 - 20</td>
<td>15</td>
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<tr>
<td>21 - 30</td>
<td>78</td>
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<tr>
<td>31 - 40</td>
<td>185</td>
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<tr>
<td>41 - 50</td>
<td>506</td>
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<td>51 - 60</td>
<td>480</td>
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<td>61 - 70</td>
<td>204</td>
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<tr>
<td>71 - 80</td>
<td>92</td>
</tr>
<tr>
<td>81 - 90</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>1568</td>
</tr>
</tbody>
</table>

### Table 2

DISTRIBUTION OF CASES AS PER MICROSCOPIC FINDINGS

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Microscopic Findings</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Inflammatory Smear</td>
<td>932</td>
<td>59.43</td>
</tr>
<tr>
<td>2.</td>
<td>Squamous Cell Carcinoma</td>
<td>548</td>
<td>34.94</td>
</tr>
<tr>
<td>3.</td>
<td>HSIL</td>
<td>67</td>
<td>4.27</td>
</tr>
<tr>
<td>4.</td>
<td>Radiation Change</td>
<td>10</td>
<td>0.60</td>
</tr>
<tr>
<td>5.</td>
<td>Inadequate</td>
<td>11</td>
<td>0.70</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1568</td>
<td></td>
</tr>
<tr>
<td>Clinical Diagnosis</td>
<td>No. of cases</td>
<td>Inflammatory</td>
<td>Carcinoma</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------</td>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Ca. Cervix</td>
<td>751</td>
<td>237</td>
<td>493</td>
</tr>
<tr>
<td>Ca Cervix post OP/RT</td>
<td>387</td>
<td>321</td>
<td>53</td>
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<tr>
<td>Unhealthy cervix</td>
<td>381</td>
<td>330</td>
<td>02</td>
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<tr>
<td>Routine pap smear</td>
<td>49</td>
<td>44</td>
<td>Nil</td>
</tr>
<tr>
<td>Total</td>
<td>1568</td>
<td>932</td>
<td>548</td>
</tr>
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Introduction:
Cervical cancer is the most common gynaecological cancer in women and is the leading cause of cancer death in women in underdeveloped countries. For over 60 years since its introduction in 1949, pap smear has been the gold standard as screening test for cervical cancer and any other lesion of cervix. It has helped enormously in the reduction of incidence of invasive cervical cancer and aided in the diagnosis, treatment and follow up of cancer cervix. As per international recommendation every women in her thirteens must have at least 1 pap smear examination annually.

Methods:
The cervical smears from Department of Pathology, Ispat General Hospital, Rourkela were studied over a period from 1st January 2013 to 31st December 2013. Reporting of the smears were done as per the Bethesda System (2001) of Reporting and results recorded. And the statistical analysis of the data was done.

Results:
Out of 280 pap smears, 174 (62%) were inflammatory lesions/cervicitis cases. 99 (35%) smears were within normal limit. 3 cases were diagnosed as carcinoma, 2 were LSIL and 1 cases each of ASCUS and HSIL found. Maximum number of patient turn over was found in the age range of 30-40 years followed by 40-50 years age group.

Discussion:
Conventional pap smears are effective in reducing morbidity and mortality from carcinoma cervix by detecting preinvasive
lesions. It is the most successful cancer screening test in the history of modern medicine.

References:
HPV (Human Papilloma Virus) is a double stranded DNA virus having 8000 base pairs in length. The complete viron consists of a DNA core and a surrounding protein capsid. It has three major regions - two protein encoded regions (Early regions and late regions) and a non-coding upstream regulatory region (URR). The early region has six open reading frames (ORFs) - E1-E7 (E3 is absent). E5, E6 and E7 encode for oncoproteins. E1, E2 causes DNA replication, E6 inhibits p53, E7 inhibits pRb. Late region contains two separate ORFs named L1 and L2 that encode for viral capsid proteins. The URR regulates transcription from early and late regions and controls production of viral proteins and infectious particles. More than 100 types identified in human and one-third of them have been sequenced. 30–40 anogenital and 15–20 oncogenic. HPV 16 and HPV 18 types account for the majority of worldwide cervical cancers. Nononcogenic types - HPV 6 and 11 are most often associated with external anogenital. Genital tract HPV are classified by their relative malignant potential as Low-Risk, High-Risk and possible high-Risk oncogenic types.

- Low oncogenic risk - 6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73, 81.
- High oncogenic risk - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82.
- Possible high oncogenic risk - 26, 66, 73 Globally, the 4 most common ‘oncogenic’ HPV types are HPV 16, 18, 45 and 31. Together, these account for ~80% of Cervical Cancer cases and HPV 16 and 18, alone, account for ~70% of Cervical Cancer cases.

Mechanism of HPV Transmission & Acquisition

- Sexual contact
  - Through sexual intercourse
Genital–genital, manual–genital, oral–genital

Genital HPV infection in virgins is rare, but may result from nonpenetrative sexual contact.

Proper condom use may help reduce the risk, but is not fully protective against infection.

**Nonsexual routes**

- Mother to newborn (vertical transmission)
- Fomites (e.g., undergarments, surgical gloves, biopsy forceps)

Hypothesized but not well documented; would be rare

Most infected individuals are unaware that they are infected and may unknowingly spread the virus.

**Pathogenesis of HPV infection**

HPV virus enters at TZ after inoc trauma of sexual intercourse. Part of HPV genome integrates into host cell DNA-expression of E6 and E7 proteins. E6 binds with p53 tumour suppressor gene and induces p53 degradation. E7 binds with another tumour suppressor gene pRb (Retinoblastoma gene product) and inactivates this protein. Both p53 and pRb function in cell cycle control and act as regulators of cell proliferation, to prevent abnormal cell division. On interaction with high risk HPV E6 and E7 the regulatory pathway of p53 and pRb is inactivated. E5 interferes with cell signaling through the EGF-receptor and disturb intercellular trafficking. These activities act as endogenous factors for development of premalignant and malignant lesions.

**Diagnostic technique of HPV**

Clinically, latent HPV infection is highly prevalent in general population. So diagnosis, particularly, of high-risk types is of great importance, as women carrying high-risk HPV infection have greater chance of developing cervical neoplasia.

Conventional diagnostic technique of cytology, histology, and colposcopy cannot detect the viruses. Cellular changes of koilocyte detection are found only in 30% of cases. In colposcopy HPV infection can be detected as flat, papillary or inverting growth. So they are not of much help neither in detection nor prediction of HPV infection and associated outcome.

Molecular biologic technique is now commonly used for HPV diagnosis. They are

1. Tissue-in-situ hybridisation (TISH)
2. Filter In-situ hybridisation (FISH)
3. Southern Blotting (dot/slot blotting)
4. Polymerase chain reaction (PCR)
   - Traditional
   - Advanced
5. Hybrid capture system (HCS) from Digene Diagnostics
6. Fast HPV (Qiagen’s test) It tests-DNA of 14 types in < than 2.5 hrs, where No refrigeration is required. Cost will be < than $5 and the equipment does not require much space. This operated with battery and best suitable for field studies.

**Treatment of HPV infection**

Treatments cannot cure HPV. But most genital HPV infections go away with the help of the body’s immune system. About 70% of HPV infections appear to go away within a year and 90% within 2 years. HPV itself cannot be treated, but the cell changes that come from an HPV infection can be treated. For example, genital warts can be treated. Pre-cancer cell changes caused by HPV can be found by Pap tests and treated. And cervical, anal, and genital cancers can be treated.
Introduction:
Group discussion is an established method to impart health education. We are organising group discussions for cancer cervix awareness since 2011. The efficacy of group discussion is better when the number of members varies from 10-15 in a group.

Methods:
During a group discussion on 12.01.2014 at Nandankanan 12 members of both sex (male 5, female-7) participated. The educational qualification of the participants were from I.A. to M.A. All the members were staying in urban areas.
A 30 minutes lecture on Cancer Cervix from etiology to prevention was delivered followed by question answer session.
Before lecture a questionnaire consisting of 10 questions related to Cancer Cervix were circulated and opinions collected. After the lecture & discussion another questionnaire consisting of 10 questions were circulated and opinions collected.

Results:
It was observed that there was definite improvement in the knowledge regarding Cancer Cervix awareness.
The existing knowledge 67% improved to 85% after the group discussion.

Conclusion:
Such type of group discussion if carried out will definitely increase awareness against cancer cervix which will propagate the message of cancer cervix eradication.

Reference:
1. Niranjan Rout, N.C. Parija, B.L. Nayak, Group Discussion - a method for cancer cervix awareness, Cancer Cervix Eradication 2011; 01: 15.
Introduction:
The Government of India implemented cancer screening under NPCDCS (National Programme for Control of Cancer, Diabetes, Cardiovascular Disease and Stroke) programme in February 2012. In April 2012 this programme was started in the Nuapada district of Odisha and gradually four more districts - Koraput, Nabarangpur, Malkangiri and Balangir were included during initial phase. Specialists of Obstetrics and Gynaecology, Surgery and Pathology along with paramedical staffs participated in the re-orientation programme on cancer screening guidelines in different phases at AH Regional Cancer Centre, Cuttack (AHRCC, Cuttack) from the above 5 districts.

Materials and Methods:
We started receiving samples for cancer screening at AHRCC, Cuttack through courier service from above said districts from January 2014. During the month January and February 2014 we have received 20 samples. The profile of the samples are as follows:
The reports were sent through E-mail to the concerned NCD Cell of the District Headquarter for information and management.

Results:
Out of the 11 pap smears 3 cases were Squamous Cell Carcinoma and 2 were suspicious.

Conclusion:
Proper implementation of NPCDCS programme in all parts of our state will definitely help to detect patients suffering from cancer cervix and other cervical pathology. Proper treatment can be provided to reduce morbidity and mortality. Also this will create an awareness among public to participate in pap smear screening programme.
Cancer Cervix is the second most common cancer among women worldwide. An estimated 550,700 new cases and 286,823 deaths due to Cancer Cervix are estimated to have occurred in the year 2010. Among all the Cervical Cancers, more than 85% cases and more than 88% deaths occur in the developing world where there is an absolute lack of proper and organized Cervical Cancer Screening programme and consequent treatment. The incidence in India varies from 20-35 per 1,00,000 women between the ages of 35 years to 64 years. On the other hand, in the developed world, the incidence is as low as 1 to 8 per 100,000 women. It is estimated that by the year 2020 the incidence will further rise and there will be 6.39 lakh cases from developing world and only 92,000 will be from the developed world.

The liberal use of Cytology and Colposcopy in the developed world has decreased the morbidity and mortality from Cancer Cervix. Cancer Cervix develops slowly after initial infection with Human Papiloma virus (HPV). It is preventable when the precursor lesions are earlier detected and actively treated. As the women do not experience any symptoms until the disease has progressed to an advanced stage, detection of precancerous and early stage are possible through Screening. It's really unfortunate that millions of women in the developing countries like India are never screened for Cervical Cancer in their entire life time. Several tests have been developed to screen women for cervical pre cancers and cancers. Each screening test has its own strength and limitations. Cervical Cytology, Visual based screening, HPV
DNA testing are the 3 important options available. In a developing country like India factors as low cost, fewer visits for screening and treatment, fewer life time screening are vital parameters for successful prevention of Cancer Cervix. The choice of the test will depend on the technical performance, cost effectiveness within the available allocated resources and socio-cultural beliefs. 

Methods of Screening:
1. Cytology(Pap Smear ,Liquid based Cytology, Autopap etc.)
2. Visual based Screening
3. HPV Testing

**1. Cytology:**
Cytology based Screening has been started since the 1950s after its invention by George Papanicolaou. It was started by the *Pap smear test* and later on modified time to time by newer methods. The drawback of traditional Pap test is its sensitivity which varies from 30-87% with very high false negative rate which means that pre-malignant and malignant cells are misdiagnosed as normal. Again the test need to be repeated at frequent interval to achieve Programmatic effectiveness. The test can be effectively implemented effectively in screening programme if infrastructure and the quality assurance of the laboratory are consistently met. It’s a major breakthrough for the developed world that its implementation for decades together has witnessed incidence and death rate has been reduced to 50%.

Over the years there has been a lot of change in traditional cytology methods in form of LBC and Automated Pap Smear method. 

*In Liquid Based Cytology (LBC)*, Cell samples are transferred to a liquid solution for mechanical separation from contaminants, sample of cells are transferred to the slide in a monolayer for review which obtains uniformity of cell population. It filters out contaminating blood, inflammatory cells & debris. It has certain advantages such as better and speeder interpretation, lower rate of Unsatisfactory smears and addition of HPV DNA testing with its remnant fluid. It is used by nearly 90% of gynaecologists in the United States since 2003. Compared to traditional Cytology no difference is found in relative sensitivity. There is also no difference found in its relative specificity when High Grade Squamous intraepithelial lesions (HSIL) and Low grade Squamous Intraepithelial lesions (LSIL) were considered.

In Automated Pap Smear Testing (Auto pap & Autocyte Screen), the material on the slide is reviewed and scored based on an algorithm. These includes variety of visual characteristics shape, optical density of the cells as to the similarity of an abnormality being present.
Autopap selects a sample of slides for manual rescreening enriched with abnormality. In autocyte screen a human reviewer after looking at various cell images determines whether a manual review is required. The reviewer needs to enter an opinion. If the findings of both the reviewer and the computer are reported as normal, no further review is needed and diagnosis is reported as “With in normal limits”.

2. **Visual Inspection Methods**:

It has been seen over the last few years that Cytology based Screening has constraints in developing world due to lack of resources, trained manpower, infrastructure and the requirement of multiple visits. So as an alternative low cost but effective screening methods based on Visual Inspection of Cervix can be done with simple equipment and relatively brief training and this has been advocated for Cervical Cancer Prevention Programme in the developing world.

From various studies done in developing countries there is comparable or greater sensitivity of Visual Inspection of the Cervix with naked eye (after application of Acetic Acid(VIA) or Lugols Iodine(VILI) than that of Cytology. One most important aspect is both medical and paramedical workers including Primary health care workers can be easily trained in the visual inspection techniques in a relative short period of time. Application of 3-5 % Acetic Acid on the Cervix causes reversible coagulation of intracellular proteins. The dysplastic and invasive cancer areas undergo maximum coagulation due to large number of undifferentiated cells which appear as Aceto-white patch. During VILI technique the principle is after application of Lugols iodine the normal squamous epithelium containing glycogen takes up iodine staining mahogany brown. The precancerous and cancerous lesions do not take up iodine due to lack of glycogen which is due to rapid division of cells so appear as well defined, thick, mustard or saffron yellow areas.

Various crosssectional studies from India, China and Africa shows that the sensitivity of VIA ranges from 67 to 79% and the specificity ranges from 49 to 86%. Various studies also mention higher sensitivity of VILI as compared to VIA however not the specificity. The results of cluster randomised control trial in southern India after a single round of screening by VIA followed by treatment in the same setting (See and Treat approach) showed a significant 25% reduction in cervical cancer incidence and a significant 35% reduction in cervical cancer mortality at the end of seven years of follow up. Another cluster randomised control trial from Mumbai on cervical cancer screening...
demonstrated a significant downstaging of cervical cancers. Various cross sectional studies also conclude that Screening with VIA and VILI should be considered where good quality cytology is not feasible and that the sensitivity of Cytology and HPV testings can be significantly increased by adding the visual test. The single visit See and Treat approach is important for programme effectiveness in developing countries where there is lots of loss of follow up cases.

3. HPV Test

Over the last decade, remarkable progress has been made in understanding Cervical Carcinogenesis. An overwhelming body of evidences show that infection with various high risk Human Papilloma Virus (HPV) is the central and necessary cause for development of Cervical Cancers & its precursor lesions. This fact was exploited for development of molecular technologies for detection of HPV DNA or RNA to overcome the limitations of Cytology as screening procedure. HPV DNA testing identifies women at risk for developing cervical neoplasia without the inherent subjectivity to cytology.

The important 4 clinical applications of detection of high risk HPV DNA are

i. As a **primary screening** test solely or **Co-test** with Cytology to detect precursor lesion

ii. As triage for women with Cytology showing ASCUS or LSIL in order to select women who need referral for colposcopic diagnosis and treatment

iii. In subsequent management of women sent for Colposcopy due to abnormal smears but where findings on Colposcopy/biopsy are negative

iv. As follow up test for women treated for high grade CIN with local ablative or excisional therapy to evaluate the treatment outcomes.

HPV DNA Testing has a higher Sensitivity and negative predictive value for detection of pre-invasive disease than cytology. But it’s important drawback is lower specificity and low positive predictive value for high grade CIN. The lower specificity is primarily due to the detection of transient infections that have not produced cellular changes. It is suggested that HPV DNA test which is more sensitive should be applied first to identify the HPV positive women. This should be followed by Cytology which is more specific. Managing HPV positive but cytology negative women is challenging. Current evidence suggest repeating screening with both cytology and HPV after one year for such women.

Several studies have shown that HPV negativity alone or in combination with negative cytology signifies a longer disease free interval against CIN 2 and 3
than being negative for cytology alone. An overview of several metaanalysis and systemic trial reviews shows minimal over-diagnosis from HPV testing for women over 30 yrs of age and the screening interval can be extended to 6 yrs with HPV DNA testing for HPV negative women.

Outcome of HPV test as a primary screening procedure (Various RCTs from Europe) states that there is definite reduction in incidence of high grade CIN 3, 5 yrs after screening. The follow up results of various randomized trials in developing world with limited resources demonstrates significant reduction in numbers of advanced cervical cancers and related deaths with HPV testing. The researchers concluded that it is the most objective and reproducible of all cervical screening tests and requires less training and quality assurance. It is beyond doubt proved to be a simple accurate and cost effective test for Primary screening in low resource countries for women more than 30 yrs of age.

LSIL and ASCUS represent the largest fraction of abnormalities in cervical cancer screening. The ASCUS-LSIL Triage study has investigated in a prospective, randomized fashion for optimal management of LSIL and ASCUS by immediate Colposcopy, HPV Triage and repeat cytology concluded that HPV Triage seemed to be at least as sensitive as immediate colposcopy in detection of high grade CIN, where need for Colposcopy referrals was halved. So HPV triage is the best strategy for management of women with ASCUS and this fact was incorporated in international guidelines. HPV Testing was also suggested to predict residual or recurrent CIN in women treated for high grade cervical lesions.

The two methods widely used for HPV detection are PCR and Hybrid Capture II (HC, Digene Corp). HC2 is a nuceic acid hybridization assay for qualitative detection of DNA of 13 oncogenic and 5 benign HPV types. It is the only HPV test approved by Food & Drug Administration (FDA) for ASCUS triage and cervical cancer screening in combination with Cytology after the age of 30 yrs. Among PCR techniques consensus PCR and type specific PCR are commonly used. Roche Amplicor HPV test is a commercial PCR based assay for HPV detection which involves a pool of 13 HR-HPV as included in HC2 assay. The most advanced HPV Genotyping approaches are more appropriate for the identification of individuals at risk of disease than its presence or absence. After consensus PCR amplifications, HPV types can be discriminated by Reverse Hybridization with type specific probes.
A new test i.e Care HPV has been developed for screening women in developing countries for CIN by detecting 14 high risk HPV types. This is one of the most simple test which can be performed by health care worker. It works on self collected sample is portable and gives prompt results within 2-5 hours which make See and Treat approach more effective. Studies from China proved that in detection of high grade CIN it is better than VIA with sensitivities and specificities of 90% and 84% respectively on self collected vaginal specimen.

SPF PCR is a commercial INNO-LiPA HPV assay which is capable of genotyping 25 different HPV types. Among the most recent tests, HPV Viral Load, HPV integration E2 status, HPV RNA detection (Pre Tect HPV Proofer) are promising for screening of Cancer Cervix for the future for developing countries.

References:
6. ASCUS-LSIL Triage study group. Results of a Randomized Trial on the management of Cytology interpretations of atypical squamous cells of undetermined significance, Am J Obstet Gynecol 2003; 188: 1383-1392
9. Wright TC. Cervical cancer screening in the 21st century: is it time to retire the
Abstract

Objective: To evaluate the inadequate pap smears (Unsatisfactory for evaluation) due to obscuring blood designated as hemorrhagic pap smears for presence of epithelial abnormalities in repeat pap testing.

Material & methods: The pap smears were categorised into ‘Satisfactory for evaluation’ or ‘Unsatisfactory for evaluation’ according to The Bethesda System, 2001 (TBS) of reporting cervical cytology. Inadequate smears may be due to paucity of cells, obscuring blood or inflammation. Those due to excess blood were repeated during a period of 2-4 weeks. The results were recorded and analysed.

Results: Total 1566 pap smears were examined, out of which 1521 (97.12%) were adequate and 45 smears (2.88%) were inadequate. There were 22 ‘Unsatisfactory for evaluation’ pap smears due to blood obscuring more than 80% of cellular morphology accounting for 1.40% of total pap smears. These patients were asked to repeat their pap testing within 2 -4 weeks. Subsequently, squamous cell carcinoma was detected in three patients and high grade squamous intraepithelial lesions in two patients.

Discussion: False negative results were found in 22.72% of inadequate (hemorrhagic) pap smears. Literature survey has revealed a false positive result in inadequate pap smears ranging between 5-50%. The cause may be blood obscuring the findings, absence of such cells in smears due to unsampling of particular...
abnormal area or non-detection of cells due to technical error.

**Key words:** False negative result, hemorrhagic pap smear, squamous cell carcinoma,

**Introduction**

The Papanicolaou test has been the mainstay of cervical cancer screening for the last 60 years. The Pap test is indicated for screening of malignant and premalignant lesions of the cervix. To obtain a consistent, reproducible and easily used system for reporting Pap smear results ‘The Bethesda system (TBS) was introduced in 1988 in a workshop held at Bethesda. It was modified in 1991 [1] and 2001.[2,3] The 2001 Bethesda System has 2 adequacy categories: “satisfactory for evaluation” and “unsatisfactory for evaluation”[1]. The “satisfactory but limited by... (SBLB)” category was eliminated. The unsatisfactory report includes reasons for the unsatisfactory designation. Any specimen with abnormal cells is by definition satisfactory for evaluation. The 2001 Bethesda System combined previous categories of “within normal limits” and “benign cellular changes” (organisms, reactive/reparative changes) into a single category, “negative for intraepithelial lesion or malignancy.”

There is very limited data on the significance of partially obscuring blood and inflammation. One study found that atypia was more likely to be present in limited smears than satisfactory smears.[4] Two retrospective case-control studies examining Pap smears from women with biopsy-proven cervical intraepithelial neoplasia (CIN) showed no significant relationship between partial obscuring factors and a false-negative report.[5,6] Prospective studies have not been done so far to establish this fact. Therefore we undertook this prospective study to evaluate the presence of false negative results in pap smears which were identified as “ Unsatisfactory for evaluation” by obscuring blood.

**Materials & methods**

All the pap smears received in Srusti Hospital, Cuttack in the period from August, 2012 till July, 2014 were categorised into –satisfactory for evaluation and unsatisfactory for evaluation. Unsatisfactory for evaluation may be due to two major reasons-1.if the slide is broken or there is paucity of well visualised squamous cells, 2.if the cells are not visualised due to obscuring blood or inflammation. All the smears which were found to be unsatisfactory for evaluation due to excess haemorrhage were repeated within 2-4 weeks and examined for detection of any epithelial abnormalities.
The previous and subsequent results were analysed and recorded.

**Results**

Total number of 1566 pap smears were examined which included 1521 (97.12%) adequate and 45 (2.88%) inadequate smears. (Table 1) Inadequate smears comprised 17 due to paucity of squamous cells, 6 due to obscuring inflammation and 22 smears were declared inadequate due to excess blood obscuring >80% of cellular morphology. The age range varied from 21 to 70 years. The reporting was done basing on The Bethesda system, 2001 and different categories included benign cellular changes (1472 or 93.99%) and 49 (3.13%) epithelial abnormalities. (Table 2)

The inadequate pap smears due to blood (hemorrhagic smears) were repeated within 2-4 weeks and in three patients squamous cell carcinoma and in two precancerous lesions (high grade squamous intraepithelial lesions-HSIL) were detected. Other smears showed features of benign cellular changes. (Table 3)

**Discussion**

The Bethesda 2001 Workshop was convened to evaluate and update the 1991 Bethesda System terminology for reporting the results of cervical cytology. A primary objective was to develop a new approach to broaden participation in the consensus process, for creating uniform terminology and for making the management by clinicians comfortable and reproducible. Instead of three categories of adequacy in pap smears, a two tiered system was accepted in 2001 TBS inclusive of ‘Satisfactory for evaluation’ and ‘Unsatisfactory for evaluation’. and eliminating the category ‘Satisfactroy but limited by .....’

An adequate papanicolaou smear is defined broadly as a properly identified glass slide with appropriate clinical history, microscopically exhibiting well preserved, well visualised good cellularity containing elements of transformation zone and without any obscuring factors like blood or exudate. If a specimen is found unsatisfactory, it will fall into two categories: rejected and not processed at all (due, for example, to a broken slide) or processed and found inadequate for other reasons (paucity of squamous cells or obscured by blood or inflammation). Any smear that contains identifiable abnormal cells should not be reported as unsatisfactory. Therefore, any cellular abnormality should be reported regardless of any limiting factors for its adequacy. (Fig.3) In our series all the unsatisfactory smears belong to second category i.e. processed but found unsatisfactory. Although this unsatisfactory category constitutes 1% to 2% of all pap tests, patients with unsatisfactory smears are
more likely to have histories of abnormalities and are at increased risk of harboring precancer or invasive cervical cancer; therefore it is important to monitor them closely.[7,8]

According to the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines for the management of patients with “unsatisfactory for evaluation” pap test results, patients should have repeated testing within 2 to 4 months.[9] The guidelines recommend repeat testing in 12 months for patients with other limiting factors such as blood or obscuring inflammation and lack of an endocervical component.[9] In the present study all the patients when asked to repeat their pap testing, agreed to do that early and the second smears were collected within two to four weeks.

Out of 1566 cervical cytology smears, 49 were inadequate accounting for 3.13%. In a study done by Kar A et al in 2005 the inadequate pap smears comprised 4.60% (228 inadequate smears from 4949 conventional pap smears ).[10] While evaluating the inadequate pap smears due to blood or exudate obscuring the cellular morphology in the range 80-100% is considered as unsatisfactory and less than that as satisfactory. For example if 50-80% of the slide is obscured by blood, it was categorised as satisfactory according to TBS 2001 (earlier satisfactory but limited by blood).(Fig.1) But if >80% is obscured by blood it was discarded and not reported upon. (Fig.2) However if any type of epithelial abnormality was found in the smear it was accepted as satisfactory and was reported. (Fig.3)

Out of the adequate smears, epithelial abnormalities accounted for 3.13 %, whereas in previous studies it was found to be 13.47% and squamous cell carcinoma was the predominant abnormality. The reasons of higher incidence in that study was because it was conducted in Cancer Institute of Cuttack and Dept. of Pathology, Cuttack. The common age group affected by squamous epithelial lesions ranged from 4th to 5th decades and in the present study also squamous cell carcinoma was the major abnormality (1.07%) of total pap smears. Inadequate smears were encountered mostly in the age group 31-50 years and hemorrhagic smears comprised 30.61% of inadequate pap smears.

Literature survey has revealed a false negative result in inadequate pap smears to be between 5%-50%. [11] The wide variation can be accounted for by different study design and by different methods of calculating the false negative rate. It is extremely difficult to determine the absolute false negative rate accurately;
most studies therefore quote relative values, based on the sensitivity of cervical screening against the final cytology report, or against histologically confirmed lesions. In the U.S. study, the false negative rate for the conventional smears was 9.4% when endocervical components were present and 16.7% when absent.[12] False-negative pap smears may result from a lesion that sheds few, if any, cells from inadequate sampling because of the location of the lesion (i.e., endocervix), from artifacts or poor preparation of slides, or from reading (interpretive) errors.[13] The use of serial pap smear screening decreases the false-negative rate; with repeated smears, the probability of false negative equals \( (0.2)^n \), where \( n \) = number of pap smears. Therefore, the probability of a false negative after 3 consecutive pap smears is \( 0.2 \times 0.2 \times 0.2 = 0.008 \), or 0.8%.[14]

Our study has shown a rate of 22.72% of positive findings in repeat pap smears which is towards upper limit of the usual range. The causes may be because the incidence of epithelial abnormalities is higher in our study and also may be haemorrhage is more common in epithelial lesions than benign cellular changes which was possibly missed during the first examination. Other reasons might be failure to sample the abnormal area, failure in transferring the abnormal cells to the glass slide even if they are sampled or rarely laboratory errors in screening or interpreting the findings.[15] Improved patient preparation or clinician technique may correct the cause of the unsatisfactory or partially obscured Pap. When there are obscuring factors, liquid-based technologies may be considered with subsequent pap tests, as liquid-based sampling generally decreases obscuring problems. Cervical samples that are preserved in a liquid suspension and prepared using the density gradient monolayer technology have many advantages over conventional cervical cytologic smear preparations. The quality of cell preservation and presentation is superior.

**Conclusion:**

In addition to other technical errors hemorrhage is found to be more common in pap smears collected from patients with squamous epithelial abnormalities which gives rise to false negative results. The incidence of inadequate smears and false negative results were found more frequently in 3rd and 4th decades of life. Therefore the authors suggest to adopt precautions in females of these age group with any suggestive history of epithelial abnormalities like presence of risk factors, bloody or foul smelling discharge and
positive finding of HPV in cervical samples.

**Reference**


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**Figure 1** - Satisfactory for evaluation. Blood obscuring <80% of cellular details. Pap stain x100

**Figure 2** - Unsatisfactory for evaluation. Pap smear due to blood obscuring >80% of cellular morphology. Pap stain x100

**Figure 3** - Hemorrhagic smear with malignant squamous cells. Considered as satisfactory for evaluation. Pap stain x100

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**Table 1** - Distribution of conventional pap smears

<table>
<thead>
<tr>
<th>Number of cases (%)</th>
<th>Adequate</th>
<th>Inadequate</th>
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<tr>
<td></td>
<td>Benign cellular changes</td>
<td>Epithelial abnormalities</td>
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<tr>
<td></td>
<td>1566</td>
<td>1472(9.5%)</td>
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**Table 2** - Age distribution of epithelial cell abnormalities in pap smear

<table>
<thead>
<tr>
<th>Age group (21-30)</th>
<th>No. of cases</th>
<th>ASCUS</th>
<th>LSIL</th>
<th>HSIL</th>
<th>SCC</th>
<th>AGUS</th>
<th>Adenocarcinoma</th>
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<tr>
<td>21-30</td>
<td>86(16.32)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>31-40</td>
<td>16(35.66)</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td>41-50</td>
<td>16(35.66)</td>
<td>0</td>
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<tr>
<td>51-60</td>
<td>16(35.66)</td>
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<tr>
<td>61-70</td>
<td>16(35.66)</td>
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**Table 3** - Follow-up findings in hemorrhagic pap smears

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<th>No. of cases</th>
<th>Follow up</th>
<th>Benign cell change</th>
<th>SCC</th>
<th>HSIL</th>
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<td>00</td>
<td>0</td>
<td>0</td>
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<tr>
<td>31-40</td>
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<td>05</td>
<td>00</td>
<td>0</td>
<td>0</td>
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<tr>
<td>41-50</td>
<td>09</td>
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<td>02</td>
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<tr>
<td>51-60</td>
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<td>04</td>
<td>01</td>
<td>0</td>
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<td>00</td>
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</table>

Kar, A et al., 2015
Introduction:
Cancer of the uterine cervix is the second most common cancer worldwide and the most common cancer in women in India. The global incidence of cervical cancer is approximately 510,000 new cases annually, with approximately 288,000 deaths worldwide. (Ref 1). Majority of patients present in the advanced stage of disease making it the most common cause of cancer related deaths worldwide. However early diagnosis and treatment can significantly improve both locoregional control as well as survival of carcinoma cervix. The paper highlights the favorable response to treatment and improved survival rates in carcinoma cervix.

Material & Methods:
Forty two patients of histopathologically proven carcinoma cervix who were evaluated and treated in the Departments of Gynec- Oncology, Oncopathology and Radiation Oncology, AH Regional Cancer Centre, Cuttack during the period March 2013 to March 2014 were analyzed. Patients of stage I to stage II A underwent surgery followed by adjuvant (postoperative) Radiotherapy or Chemoradiotherapy as per indications while patients of stage II B onwards were treated with Chemoradiation as the definitive therapy. Radiotherapy included External Beam Radiotherapy to a dose of 50 Gy in 25 #, 5 # per week over 5 weeks followed by 3 # of Brachytherapy, 7 Gy per #, once a week. Chemotherapy included weekly injection Cisplatinum (40 mg/m²) given every Monday, 5 such cycles as a radiosensitiser. The toxicity and compliance was evaluated every Tuesday on a weekly basis. Response was assessed after completion of External Beam Radiotherapy, then 1 month after completion of treatment and every 2 months thereafter.
Results:
The age range of the study population was from 20-75 years. Majority of the patients i.e. 57 % presented in the 6th decade (51-60 years) followed by 12 % patients who presented in the 5th decade (41-50 years). Most of the patients at presentation were locally advanced i.e. stage IIB to stage IV (90.38 %). 52.38 % of patients presented in stage III itself. Only 4 out of 42 patients presented in early stage (stage I to Stage II A) and were therefore operable. The histopathology of 38 out of 42 patients i.e. (90.7 %) was squamous cell carcinoma while 4.76 % patients had adenocarcinoma. (Table1)

Out of these 4 patients who underwent surgery 3 showed high risk features in the postoperative histopathology report and were therefore treated with adjuvant chemoradiation. The other patient was treated with adjuvant radiation alone. All 38 patients of locally advanced carcinoma cervix were treated with concomitant chemoradiation. 61 % of patients completed the planned 5 cycles of weekly Injection Cisplatinum. 78.57 % patients completed the entire treatment within the stipulated time period of 8 weeks. 14.2 % of patients delayed treatment upto 9 weeks and the remaining 7.14 % protracted treatment beyond 9 weeks. (Table2)

The Post Treatment Response was evaluated 1 month after completion of treatment, every 2 months thereafter. With a median duration of follow up of 12 months, 76.2 % patients are surviving without disease, 4.8 % patients are surviving with disease, 7.14 % patients have developed distant metastases, 7.14 % patients were lost to follow up and 4.7 % patients died due to disease. (Table3)

Discussion:
Carcinoma of the uterine cervix is the most common cancer among females worldwide and is a major cause of cancer related mortality. In the West early detection through regular screening has significantly controlled the prevalence of the disease and Pap smear has reduced deaths due to carcinoma cervix by three fourths in the United States. However, in India, majority of patients present in the advanced stage. As seen in the present article 90.7 % of patients were in locally advanced stage (stage IIA to stage IV). As per NCI (National Cancer Institute) Feb 1994 recommendations, these patients are treated with concomitant chemoradiation with weekly injection Cisplatin.² The patients in the early stage (7.4%) showed high risk features in the postoperative histopathology report like Lymph Node involvement, Margin positivity and Parametrium infiltration and were thus
treated with postoperative/adjuvant chemoradiation. In the present article most of the patients i.e. 60.97% could complete 5 cycles of weekly Cisplatin. Cisplatin in carcinoma cervix acts as a radiosensitiser and sensitizes the cells to the lethal damage of radiation. The stipulated time period for treatment of carcinoma cervix is a maximum of 8 weeks. According to NCI, for every 1 day of treatment time protraction beyond 8 weeks, locoregional control decreases by 1%.\(^3\)

In the present article majority of patients i.e. 78.57% completed treatment within 8 weeks while 7.14% patients delayed treatment beyond 9 weeks. The treatment delay here was largely due to noncompliance and logistics of the patients.

Patients were assessed after External Beam Radiotherapy for feasibility of Brachytherapy and next 1 month after completion of treatment for response evaluation. With a median duration of 12 months follow up, 32 patients i.e. 76.2% of patients were found to be locoregionally controlled. Another 4.8% patients were surviving with the disease while 3 patients (7.14%) developed distant metastases. On subset analysis and correlation it was found that patients who developed distant metastases had presented in stage IV-A. This finding confirms that advanced stage of the disease at presentation carries a poor prognosis.

At 12 months of follow up, 76.2% of patients being locoregionally controlled claims that carcinoma cervix shows a favorable response to treatment in early stages. The response rate is an encouragement for all patients to receive appropriate treatment.

**Conclusion:**
Carcinoma of the uterine cervix is the most common cancer among females in India. Pap smear is an effective screening tool which helps to catch the disease in early stage. Early diagnosis and treatment can improve locoregional control and survival of carcinoma cervix patients. With a median duration of follow up of 12 months the present manuscript highlights the fact that cancer cervix is curable if treated early.

**References:**
3. Overall treatment time in advanced cervical carcinomas: a critical parameter in

**Table 1: Demographic & Clinicopathological parameters**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N=42</th>
<th>%</th>
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<tr>
<td>21-30</td>
<td>1</td>
<td>2.4</td>
</tr>
<tr>
<td>31-40</td>
<td>1</td>
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</tr>
<tr>
<td>41-50</td>
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<td>10</td>
<td>24</td>
</tr>
<tr>
<td>71-80</td>
<td>1</td>
<td>2.4</td>
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<tr>
<td><strong>Stage (FIGO)</strong></td>
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<td>%</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
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</tr>
<tr>
<td>II A</td>
<td>3</td>
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<tr>
<td>IIB</td>
<td>11</td>
<td>26.1</td>
</tr>
<tr>
<td>III</td>
<td>22</td>
<td>52.38</td>
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<td>IV</td>
<td>5</td>
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<tr>
<td><strong>Histopathology</strong></td>
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<tr>
<td>Squamous cell carcinoma</td>
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<td>Adenocarcinoma</td>
<td>2</td>
<td>4.76</td>
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<tr>
<td>Others</td>
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Abstract

Cervical cancer is the fifth most common cancer in humans, the second most common cancer in women worldwide and the most common cause of cancer death in females in the developing countries. Since its introduction in 1949, pap smear has been the gold standard screening test for cervical cancer. The aim of our study was to analyse the number of pap smears studied during 2013 at the Department of Pathology, AHRCC, as per their age, clinical presentation and microscopic findings as well as to find out the incidence of carcinoma cervix and post operative and post-irradiation follow up of the cases.

Keywords: Cancer Cervix, Pap smear.

Carcinoma of cervix is a major global health problem and is the second most common cancer among women with an estimated 493,000 new cases and 274,000 deaths occurring annually all over the world.\(^1\) Current estimate indicates that every year about 5 lakh new cases of cancer cervix are diagnosed worldwide of which approximately 1.4 lakh cases occur in India. Now about 75,000 women die due to cervical cancer in India, but in developed countries like USA, UK the death rate is negligible. Recently WHO has classified carcinoma cervix as a preventable disease. Secondary prevention based on cervical paper smear screening has been successful in many developed countries.

The widespread introduction of cervical screening by papanicolaou test, or pap smear has given dramatic result in
reducing the incidence and mortality rate of cancer cervix in developed countries.\textsuperscript{2} Pap smear screening in every 3-5 years with appropriate follow up can reduce cervical cancer incidence by up to 80\%\textsuperscript{3} Unfortunately many developing countries lack the awareness and facility to carry out widespread pap screening.\textsuperscript{4,5}

**Material and Methods**

Cervical smears collected in the Gynaecological Oncology Department of AHRCC during Jan-Dec. 2013 were received in the Department of pathology, AHRCC and pap staining was done. Age and clinical details of patients were recorded. The slides were examined and results were recorded. Analysis of observations were made and compared with age and clinical details.

**Results :**

Out of 1187 pap smears studied in the year 2013, maximum number of cases were in fifth decade of life. Inflammatory smears were found in 467 (39.3\%) cases, 548 cases (46.16\%) were squamous cell carcinoma, 67 (5.64\%) cases were suspicious smears/HSIL cases and radiation changes were observed in 10 (0.8\%) cases. Only 11 cases (0.9\%) were inadequate on haemorrhagic smears.

Out of 224 post treatment (post op and post RT) follow up cases radiation change was found in 17 cases.

Out of 646 cases clinically diagnosed as carcinoma cervix 491 were positive for carcinoma microscopically.

**Discussion :**

Carcinoma cervix is preceded by a prolonged premalignant or non-invasive phase, (may range up to 20 years). During that period the premalignant or intraepithelial lesions shed abnormal cells. These cells can be detected by pap smear. This is of utmost importance which reduces the incidence of carcinoma cervix.

Dr. George Nicholas Papanicolaou is said to be the father of Cytology since he could detect first cancer cells in the vaginal smears of cancer cervix patient in 1923. After long years of his dedicated hard work he published “new cancer diagnosis” in which the importance of pap smear test was mentioned in detail. Then the pap test was accepted and became a routine practice for screening and diagnosis and follow up in cancer cervix patients. Since its introduction in 1949, it has helped in reducing the cervical cancer mortality rates roughly to half.\textsuperscript{6}

There are various risk factors responsible for the development of cancer cervix. Out of which the most important cause established now is human papilloma virus infection, along with other factors like early age at marriage, multiple sexual...
partners, multiparity and low socioeconomic status etc. 7-8
Study conducted during 2010, 2011 and 2012 at AHRCC showed maximum number of patient turnover is within age range of 40-60 years. 9,10,11 Our present study also correlates with it.

**Conclusion:**
For the reporting of pap smears, internationally The Bethesda System (2001) of reporting is followed, which includes specimen adequacy and nature of epithelial cell abnormality. It has been decided internationally that every woman above the age of 30 years must have at least one pap smear examination to detect any epithelial cell abnormality. Pap smear is very useful in prevention, detection and in post treatment follow up of cancer cervix.

**References:**
11. Sasmita Panda, Adyasha Mohapatra, Sagarika Samantaray, N. Rout,
Bhagyalaxmi Nayak, Sushil Kumar Giri,
Clinico-cytological pattern of pap smear at

Table – 1 Age distribution of cases

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<thead>
<tr>
<th>Age group</th>
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<td>10 - 20</td>
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<tr>
<td>21 - 30</td>
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<tr>
<td>Total</td>
<td>1187</td>
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Table - 2

<table>
<thead>
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<th>DISTRIBUTION OF CASES AS PER MICROSCOPIC DIAGNOSIS</th>
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<tbody>
<tr>
<td>BENIGN</td>
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<td>INFLAMATORY</td>
</tr>
<tr>
<td>CERVI CITS</td>
</tr>
<tr>
<td>ENDOCER VICAL POLYP/GROWTH</td>
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<tr>
<td>ATROPHIC VAGINATIS</td>
</tr>
<tr>
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<td>LSIL</td>
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<tr>
<td>SQ. CELL CA.</td>
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<td>ADENO. CA</td>
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<tr>
<td>OTHERS</td>
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<tr>
<td>R.CHANGE</td>
</tr>
<tr>
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Abstract
Cervical cancer is the second most common cancer in female population worldwide and the leading cause of cancer death in females in developing countries. Screening for cervical cancer through Pap smears has been gold standard ever since its introduction in 1949. The aim of current study was to analyse the number of pap smears studied in the year 2013 at department of Pathology, Ispat General Hospital, Rourkela. The study intended to examine the agewise distribution of cervical lesions, neoplastic as well as non-neoplastic.

Keywords: pap smear, cancer cervix, cervicitis.

Introduction:
Carcinoma cervix is a major health problem, being the second commonest tumour prevalent in females. Current estimates indicate more than 5 lakh cases new cases are diagnosed every year worldwide. Approximately 1.5 lakh cases are diagnosed from India. Almost half of these cases die due to cervical cancer. Data from developed countries show negligible deaths due to cervical cancer. Cervical screening has proved successful in early diagnosis and thus earlier interventions. WHO has hence classified carcinoma cervix a preventable disease.

Papanicolaou stain was introduced in 1949 for cervical cytology; since then it has been the gold standard worldwide. Conventional smears and Liquid Based Cytology have together increased the sensitivity and positive predictive value of Pap screening. Recent data suggests Pap
screening done every 3 years (conventional) and 5 years (LBC) can reduce cervical cancer incidence by up to 80%.

**Material & Methods**

The cervical smears received at Department of Pathology, Ispat General Hospital from January 1st, 2013 to December 31st, 2013 were studied and reported as per Bethesda system of reporting (2001). The results were recorded and statistical analysis was done. (Table-1)

**Results**

Out of 280 adequate smears received at our institute, 174 cases (62%) were inflammatory lesions of cervix and vagina. 99 (35%) cases were reported within normal limits. One case each of ASCUS, LSIL, HSIL, Squamous cell carcinoma were reported. No case of adenocarcinoma was reported.

Inflammatory smears were mostly reported during 31-40 years of age. Maximum patient turnover was noted in the age group of 31-50 years. One case each of LSIL, HSIL and Squamous Cell Carcinoma and ASCUS were reported in the age group of 41-50 years. Most smears were inflammatory in patients above 50 years.

**Discussion**

Cervical cancer is the second most common cancer in females. Pap stain has evolved as a gold standard screening technique. A normal diagnosis given on routine conventional Pap warrants next screening after 3 years. Literature suggests that this time interval can be increased to 5 years in case of LBC smears.

Our current study shows that maximum number of patients undergoing Pap screening test show cervicitis or vaginosis. Most of the women taking the test belong to 31-50 age group. This age group also shows an inclination towards precursor malignant lesions of squamous and glandular cells.

Many developing countries do have adequate resources and lack the awareness towards need of widespread Pap screening. However after 50 years the frequency of screening should be increased to one test annually as incidences of atypical findings increase multiple fold. However we can see that fewer women of this age group come for cervical screening.

One possibility may be increased cases of total hysterectomy in post menopausal women for varied gynaecological indication. General awareness against cervical cancer amongst general public and efforts to encourage post menopausal women who have not
undergone hysterectomy, to undergo cervical screening test is needed.

![Table 1: Age Wise Distribution of Cervical Lesions]

<table>
<thead>
<tr>
<th>Age Group</th>
<th>WNL</th>
<th>Vaginosis &amp; Cervicitis</th>
<th>ASCUS</th>
<th>LSIL</th>
<th>HSIL</th>
<th>Sq. cell carcinoma</th>
<th>AGUS</th>
<th>Adeno carcinoma</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>11</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>31-40</td>
<td>44</td>
<td>66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>110</td>
</tr>
<tr>
<td>41-50</td>
<td>27</td>
<td>54</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>85</td>
</tr>
<tr>
<td>51-60</td>
<td>11</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td>&gt;60</td>
<td>6</td>
<td>22</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>99</td>
<td>174</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>280</td>
</tr>
</tbody>
</table>

**Conclusion**

The Bethesda System (2001) is accepted internationally for Pap smear reporting of cervical lesions. It includes sample adequacy and nature of epithelial cell abnormality. The incidence of cervical cancer has decreased more than 50% in the past 30 years because of widespread screening by cervical cytology thus highlighting the importance of Pap smear in prevention, detection, and post treatment followup of patients.

**References**

Introduction:
The hepatitis B virus (HBV) and human papilloma virus (HPV) are tissue specific DNA viruses that infect hepatocytes and basal squamous epithelial cells, respectively. Chronic infections with the HBV and high risk HPVs are important risk factors for hepatocellular carcinoma (HCC) and cervical cancer, respectively. Both HPV and HBV are transmitted by sexual contact. The present study is designed to know the incidence of simultaneous infection by both viruses.

Methods:
Samples for Pap Test & blood for HBsAg examination were collected from 11 different patients in the Gynaecologic Oncology Department of AHRRCC, Cuttack in the month of October 2013. The conventional pap smears were examined for presence of koilocytes, a crude indicator for HPV infection and the blood samples were examined for HBsAg by strip ELISA kits.

Results:
The profile of the samples are as follows:
- Pap Test - 11 cases
  - Inadequate smear - 3
  - Inflammatory - 4
  - Suspicious - 1
  - Squamous cell carcinoma - 3
- HBsAg - 11 cases
  - Positive - Nil
  - Negative - 11 cases

Discussion:
Both viruses, HPV and HBV, frequently integrate into the human host genome. Chronic HPV infections are associated with the development of HCC and chronic HPV infections with the development of cervical cancer and squamous cell carcinoma of head & neck. During this study we could not detect koilocytes in pap smear and also HBsAg tests indicated absence of HBV infections.
Further study with large samples are required to opine on this pilot study.

References:
Introduction:
Group discussion is an established method to impart health education. We are organising group discussions for cancer cervix awareness since 2011. The efficacy of group discussion is better when the number of members varies from 10-15 in a group.

Methods:
During a group discussion on 1.03.2015 at Chandikhole 14 members participated. The educational qualifications of the participants were two level. All the members were staying in areas. A 30 minutes lecture on Cancer Cervix from etiology to prevention was delivered followed by question answer session. Before lecture a questionnaire consisting of 10 questions related to Cancer Cervix were circulated and opinions collected. After the lecture & discussion another questionnaire consisting of 10 questions were circulated and opinions collected.

Results:
It was observed that there was definite improvement in the knowledge regarding Cancer Cervix awareness. The existing knowledge 71% improved to 83% after the group discussion.

Conclusion:
Such type of group discussion if carried out will definitely increase awareness against cancer cervix which will propagate the message of cancer cervix eradication.

Reference:
1. Niranjan Rout, N.C. Parija, B.L. Nayak, Group Discussion - a method for cancer cervix awareness, Cancer Cervix Eradication 2011; 01: 15.
Introduction:
The Government of India implemented cancer screening under NPCDCS (National Programme for Control of Cancer, Diabetes, Cardiovascular Disease and Stroke) programme in February 2012. In April 2012 this programme was started in the Nuapada district of Odisha and gradually four more districts - Koraput, Nabarangpur, Malkangiri and Balangir were included during initial phase. Specialists of Obstetrics and Gynaecology, Surgery and Pathology along with paramedical staffs participated in the re-orientation programme on cancer screening guidelines in different phases at AH Regional Cancer Centre, Cuttack (AHRCC, Cuttack) from the above 5 districts.

Materials and Methods:
We started receiving samples for cancer screening at AHRCC, Cuttack through courier service from abovesaid districts from January 2014. During the year 2014 we have received 72 samples. The reports were sent through E-mail to the concerned NCD Cell of the District Headquarter for information and management.

Results:
Out of the 37 pap smears 05 cases were Squamous Cell Carcinoma and 28 cases were inflammatory (Table-1).

Discussion:
Collection of conventional pap smear at peripheral hospital & despatching them to the central hospital for evaluation is a useful procedure for pap smear examination. This not only helps to serve the patient at their door step but also creates awareness among neighbours to undergo pap test.
Conclusion :
Proper implementation of NPCDCS programme in all parts of our state will definitely help to detect patients suffering from cancer cervix and other cervical pathology. Proper treatment can be provided to reduce morbidity and mortality. Also this will create awareness among public to participate in pap smear screening programme.

Reference :
Piver type III radical hysterectomy is the standard treatment of choice for International Federation of Gynecology and Obstetrics (FIGO) stage IB to IIA cervical cancer, with a high 5-year overall survival rate of over 80%. But this type of radical surgery usually cause urinary dysfunctions, such as bladder hypotonia, urinary incontinence, and abnormal sensation, in 12% to 85% of patients which are due to damage to the pelvic nerve plexus (inferior hypogastric plexus) and its vesical branches. Furthermore, anorectal dysfunctions, including constipation, have been reported in 5% to 10% of patients. Sexual dysfunctions, including decrease in sexual interest and orgasm, and vaginal dryness, are common after radical surgery, which compromise sexual activity leading to anxiety and distress. These complications lead to evolve an alternative technique of Radical Hysterectomy where the nerves responsible for bowel, bladder and sexual functions are spared which is called Nerve Sparing Radical hysterectomy. Over the years there have been a lot of modifications of this procedure to improve the quality of Life with preservation of vitals nerves. This procedure has been included in the new classification of radical hysterectomy proposed by Querleu and Morrow in 2008. However, this nerve-sparing technique still needs improvement and simplification because it is too complicated and extra skill is required to perform. In the past few years Nerve Sparing Radical Hysterectomy has been developed to overcome these complications.
sparing radical surgery has been modified to a more simpler approach called Nerve plane sparing radical surgery which is characterized by integral preservation of the autonomic nerve plane. During this modified procedure, the nerve plane (meso-ureter and its extension) containing most of the autonomic nerve structures was integrally preserved.

Urinary, anorectal, and sexual dysfunctions are caused by injury of the pelvic autonomic nerves during radical surgery. These nerves play a major role for the neurogenic control of urinary and anorectal functions. Moreover, they supply blood vessels of the female genital tract and thereby affect sexual activity by neurogenically controlling its lubrication or swelling response. Thus, nerve-sparing radical surgery (NSRS) has emerged in the last 30 years by Japanese Onco-surgeons for reducing surgery-related dysfunctions as pelvic autonomic nerves are preserved (Tokyo method) without compromising oncologic outcomes. In this procedure, the hypogastric nerves, instead of the pelvic nerve plexus and its vesical branches, are preserved at several steps during a classical radical hysterectomy. Consequently, the hypogastric nerves constitute the main anatomical landmark of nerve-sparing radical hysterectomy because they form the upper limit of the pelvic nerve plexus and the vesical branches. Japanese gynaecologists focused their attention on the cardinal ligament of the uterus rather than that of the parametrium. Once the pararectal and paravesical spaces are developed, the cardinal ligament appears clearly between the two spaces. Japanese gynaecologists identified two parts in the cardinal ligament, i.e. the vascular part and the ‘nerve’ part. They believed that the neural part of the cardinal ligament contained the pelvic splanchnic nerves. The pelvic splanchnic nerves running along the cardinal ligament are shown in a figure below which was prepared by a Western gynecologist. Therefore, in the context of nerve-sparing treatment, the cardinal ligament has become one of the critical issues for the surgical procedure, at least in Japan. It is only recently that nerve-sparing radical hysterectomy has been introduced to Western as well as to Asian countries. Thus, it took a surprisingly long time for the ‘Tokyo method’ to gain acceptance elsewhere in the world.

During this nerve sparing procedure, individual autonomic nerve structures were identified and separated by meticulous dissection in surgical tissue planes. After

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Padhy, A.K et al., 2016
excision of the cardinal ligament, the branches of the pelvic splanchnic nerves were identified and dissected beneath the deep uterine veins. Subsequently, hypogastric nerves on the lateral side of the uterosacral and rectovaginal ligaments were identified and dissected, and the ligaments were then divided near their roots. In the paracolpium, the nerve fibers from Hipogastric Nerves and Pelvic Splanchnic Nerves intermingle to form the inferior hypogastric plexus, which stretches the uterine and bladder branches. During excision of the paracolpium, the uterine branch was transacted. The fan-shaped bladder branch was then carefully identified, separated from the posterior leaf of the vesico-uterine ligament, and lateralized.

However, the efficacy and safety of NSRS are still controversial in comparison with conventional radical surgeries despite a growing number of studies addressing the issue of NSRS. In particular, major limitations are no consensus on which part of the uterine-supporting ligaments the nerve-sparing technique should be directed to, an unresolved concern about whether NSRS may interfere with radicality necessary for treating cervical cancer, and a debate on the discrepancy in prognosis between conventional radical surgery and NSRS.

Although three prospective randomized controlled trials (RCTs) and one systematic review with a meta-analysis have been published up to now, they are not enough to clarify the efficacy and safety of NSRS in cervical cancer due to small numbers of enrolled patients. Thus, this meta-analysis was performed to compare clinical outcomes, and urinary, anorectal, and sexual dysfunctions between Conventional Radical Surgery and Nerve Sparing Radical Surgery in patients with early-stage cervical cancer which concluded that this procedure is feasible and safe, except possibly when used with very obese patients and patients with broad, bulky tumors. Surgical preservation of the pelvic autonomic nerves in radical hysterectomy deserves consideration in the quest to improve both cure and quality of life in cervical cancer patients.

References:


Abstract:
In developing countries, there is a lack of effective screening programs for cervical cancer. In these countries, no clinically significant reduction in the incidence of cervical cancer has occurred during the past three decades. In developed countries, by contrast, there has been a major decline in cervical-cancer mortality after the introduction of large-scale cervical cytologic testing. The aim of the study is to analyse the total number of pap smears examined in the year 2014 at S.C.B. Medical College, Cuttack and stratify them with respect to their age, presentation and microscopic varities as neoplastic and nonneoplastic lesions of uterine cervix.

Key words: pap smear, cancer cervix.

Introduction:
Cervical cytology programme was introduced in 1988 with a clinical hope that the mortality and morbidity associated with cervical cancer could be decreased. But still cervical cancer is the second most common malignancy among females in a developing country like India[1]. Current data shows about 500,000 new cases are diagnosed annually and 50 % of mortality occurs in Asia. Among different countries in Asia, highest prevalence of cervical cancer was observed in India[2]. The cervical cancer burden in India alone was estimated as 100,000 in 2001 AD. Incidence of cervical cancer is decreasing due to availability of infrastructure and facilities for early diagnosis in advanced counties but it is still a major problem in India. The first presentation of patients of cervical cancer in most cases in India is observed at an advanced stage which ultimately leads to a high mortality and morbidity.

Human papillomavirus (HPV) infection appears to be involved in the development of more than 90% of cases of cervical cancer[3]. HPV vaccines protect against...
many high-risk strains of this family of viruses and may prevent up to 90% of cervical cancers \cite{4,5}. Guidelines recommend continuing regular pap smears beyond the age of 30 years to identify precancerous changes which when treated can prevent the development of cancer.

**Material & method:**
Cervical smears were collected in the O&G Department of S.C.B. Medical College by an Ayre’s spatula from the squamo-columnar junction of cervix and fixed with absolute alcohol. It is then sent to the Pathology Department of S.C.B. medical college during the period from January 2014 to December 2014. Age and clinical details were recorded. Slides were stained with papanicolaou stain and examined microscopically and the results were recorded. Analysis of observations was done by comparison of age and clinical details.

**Results:**
Out of 2680 adequate pap smears collected in 2014, 2591 were negative for intraepithelial lesions and malignancy. Majority of those smears i.e. 2081 (77.6%) were suggestive of inflammatory lesions of cervix and vagina in addition to 510 (19.02%) cases showing various reparative changes (Table 2). 9 (0.33%) cases of LSIL, 25 (0.93%) cases of HSIL, 34 (1.26%) cases of squamous cell carcinoma and 34 (0.78%) cases of adenocarcinoma were reported.

Maximum number of patients belonged to the age group of 41 – 50 years of age (Table 1). Squamous cell carcinoma was mostly observed in the 41 – 50 years and more than 60 years of age group (Table 3). HSIL cases were more commonly encountered than LSIL cases.

**Discussion:**
Though carcinoma of cervix is one of the leading causes of death in females, we can overcome this problem by regular screening procedure like pap smear examination. In the west, the incidence of carcinoma cervix is greatly reduced due to
regular screening. But in India, majority of the females present at an advanced stage due to lack of awareness.

Our current study shows that maximum number of patients shows cervicitis and vaginosis belonging to the third and fourth decades of age group. Human papillomavirus infection is the most common factor for the development of squamous cell carcinoma. Pap smear examination must be carried out every 3–5 years during reproductive age group with appropriate follow-up which can reduce cervical cancer incidence up to 80%[6]. Abnormal results may suggest the presence of precancerous changes, allowing examination and possible preventive treatment. The HSIL data from less-developed countries remain scarce as HSIL detection requires active cervical screening, which is rare in such settings.

In India, the number of people with uterine cervix cancer is rising, but overall the age-adjusted rates are decreasing [7]. Regular screening has meant that precancerous changes and early-stage cervical cancers have been detected and treated early. Also at the levels of periphery hospitals, collection of pap smears and despatching them to the central hospitals will serve the patients at their door steps and will also create awareness among neighbours to undergo the screening pap examination.

Conclusion:
Bethesda system (2001) of pap smear reporting has been accepted internationally for the reporting of cervical lesions[8]. The adequacy of sample and the abnormal cells are reported. Any specimen containing abnormal cells is by definition satisfactory for evaluation. Early diagnosis and regular screening may catch hold the susceptible patients at an early stage and result in proper management of cases with downstaging of cancer cervix.

References:

7. National Cancer Registry Programme under Indian Council of Medical Research Reports.

Introduction:
Carcinoma of cervix is a major global health problem and is the second most common cancer among women with an estimated 493,000 new cases and 274,000 deaths occurring annually all over the world.\(^1\) WHO has classified carcinoma cervix as a preventable disease. Secondary prevention based on cervical paper smear screening has been successful in many developed countries.

The widespread introduction of cervical screening by papanicolaou test, or pap smear has given dramatic result in reducing the incidence and mortality rate of cancer cervix in developed countries.\(^2\) Pap smear screening in every 3-5 years with appropriate follow up can reduce cervical cancer incidence by upto 80%.\(^3\)

Unfortunately many developing countries lack the awareness and facility to carry out widespread pap screening.\(^4,5\)

Material and Methods
Cervical smears collected in the Gynaecological Oncology Department of AHRCC during Jan-Dec. 2014 were received in the Department of pathology, AHRCC and pap staining was done. Age and clinical details of patients were recorded. The slides were examined and results were recorded. Analysis of observations were made and compared with age and clinical details.

Results :
Out of 1307 pap smears studied in the year 2014, maximum number of cases were in fifth decade of life. Inflammatory smears were found in 400 (30.6%) cases, 837 cases (64%) were squamous cell carcinoma, 70 (5.3%) cases were suspicious smears.

Discussion :
Carcinoma cervix is preceded by a prolonged premalignant or non-invasive phase, (may range upto 20 years). During that period the premalignant or
intraepithelial lesions shed abnormal cells. These cells can be detected by pap smear. This is of utmost importance which reduces the incidence of carcinoma cervix. There are various risk factors responsible for the development of cancer cervix. Out of which the most important cause established now is human papilloma virus infection, along with other factors like early age at marriage, multiple sexual partners, multiparity and low socioeconomic status etc.6-7

### Conclusion:

For the reporting of pap smears, internationally The Bethesda System (2001) of reporting is followed, which includes specimen adequacy and nature of epithelial cell abnormality. It has been decided internationally that every woman above the age of 30 years must have at least one pap smear examination to detect any epithelial cell abnormality. Pap smear is very useful in prevention, detection and in post treatment follow up of cancer cervix.

### References:

Group Discussion - A novel method for cancer cervix awareness

Niranjan Rout
A.H. Regional Cancer, Cuttack

Introduction:
Group discussion is an established method to impart health education. We are organising group discussions for cancer cervix awareness since 2011. The efficacy of group discussion is better when the number of members varies from 10-15 in a group.

Methods:
During a group discussion on 28.06.2015, twenty-three members participated in two groups. All the members were staying at Bhubaneswar and belong to one NGO. A 30 minutes lecture on Cancer Cervix from etiology to prevention was delivered followed by question answer session. Before lecture a questionnaire consisting of 10 questions related to Cancer Cervix were circulated and opinions collected. After the lecture & discussion another questionnaire consisting of 10 questions were circulated and opinions collected.

Results:
It was observed that there was definite improvement in the knowledge regarding Cancer Cervix awareness. The existing knowledge 51.3% improved to 83% after the group discussion.

Conclusion:
Such type of group discussions if carried out will definitely increase awareness against cancer cervix which will propagate the message of cancer cervix eradication.

Reference:
1. Niranjan Rout, N.C. Parija, B.L. Nayak, Group Discussion - a method for cancer cervix awareness, Cancer Cervix Eradication 2011; 01: 15.
CANCER CERVIX ERADICATION

An Awareness Initiative

MESSAGE
Cancer Cervix Eradication Day Massage

Dr. P. C. Mahapatra
Professor, O & G
S.C.B. Medical College, Cuttack
PRESIDENT, FOGSI

Message: 2011

Cancer Cx is one of the leading causes of cancer of the genital tract in country like India. There has been a tremendous advances in the understanding of histogenesis, etiological factors and changing trends in screening modalities and techniques of surgical management during the last decade or so.

The strong association of HPV infection and the emergence of HPV vaccines has proved to be one of the landmark research in preventing Ca Cx in the community, which needs awareness as well as propagating the scientific knowledge in this regard.

“Vaccinating the adolescent daughters and screening the mothers” should be the slogan in coming years.

I congratulate the members and office bearers of Odisha Chapter of Cytologists for their untiring efforts in creating awareness and spreading the novel concept to the healthcare providers as well as beneficiaries.

(Dr. P.C. Mohapatra)
Prof. N. C. Parija
President IAPM - 2011 &
President Odisha Chapter (I.A.C.)

Message: 2011

I am extremely delighted that our Odisha chapter of Indian Association of Cytologists (I.A.C.) in collaboration with ABC Foundation is going to celebrate the “Cancer Cervix Eradication Day”. This day is observed as the birth day of Dr. George Papanicolaou, inventor of the Pap smear. He invented such test in 1920 and was thrilled to identify the first cancer cells in the vaginal cytology smear of uterine cervix. The test gained popularity in West and saved millions of life of women from death of cancer cervix. Dr. Papanicolaou published a famous monographs "Diagnosis of Uterine Cancer by the vaginal smear”. It has become immense help to the Gynecologist, Pathologist and Cytologist to screen out cancer cervix patients and to reduce the morbidity and mortality rate of cancer cervix. This test has not gained popularity in our country though nine decades have passed away. Now it is the duty of our friend doctors as well as N.G.O’S to create awareness about the importance of this simple test which can prevent or eradicate cancer cervix.

I express my deepest gratitude and best wishes to the organizers specially Prof. N. Rout for its memorable success.

Thanks.

(Dr. N. C. Parija)
I am happy to know that the Odisha Chapter of Indian Academy of Cytologists in collaboration with ABC Foundation is going to celebrate the Cancer Cervix Eradication Day. This attempt of awareness programme will motivate the common woman of our society to undergo pap test regularly by which early diagnosis and treatment of cancer cervix will be possible and will facilitate to reduce the morbidity & mortality. I wish all success of the programme.

( Dr. Kanaklata Dei)
Prof. Dr. Badal Mohanty

M.D. (Delhi), F.I.C.S., F.I.C.O.G.
Dip. Lap. Surgery (Germany)
Gynaecologic cancer surgeon Laparoscopy surgeon
Formerly –
Professor & Head of Gynaecologic Oncology
A.H. Regional Cancer Centre, Cuttack
President, Association of Gynaecologic Oncologists of India
Visiting Consultant :
Kalinga Hospital, Bhubaneswar

Message

Over all those past years efforts from people, society and authority round the world has succeeded in past for almost making Cancer Cervix a disease of past.

In India we have trying for half a century and has still a long way to go to make cancer cervix a thing of the past.

Not to put every burden on the Government to do everything for us let us do a little to propagate cancer vaccination and pap smear examination mandatory for our daughters and mothers.

(Prof. Dr. Badal Mohanty)
“Cancer Cervix is Preventable, yet to be prevented”

Cancer cervix ranks first among all Gynaecological malignancies. Most of the patients present in advanced stages of the disease. Lack of health education about the cause and its prevention by way of screening by pap test and VIA are important factors responsible for late stage presentation as evidenced from different studies.

I am glad to know that the ABC Foundation of Cuttack has come forward to contribute their effort to organise such awareness programmes to educate public. Their approach through group discussions with public for the disease awareness and organisation of CME & workshops for medical personnel alongside publication of the Journal “Cancer Cervix Eradication - An awareness initiative” are commendable one.

I wish all success in their endeavour.

(Dr. S.K. Giri)
F200, German Cancer Research centre (DKFZ)
Foundation Under Public Law
Im Neuenheimer Feld 280
69120 Heidelberg
Germany

Message

Dear Prof. Rout,

Thank you very much for your e-mail of Febr. 16. Of course, I am profoundly honored to label my birthday, the 11th of March as “Cancer Cervix Eradication Day” at your place. I am also very honored for the oration dedicated to my name. Certainly I do hope that your activities will lead to a better prevention of cervical cancer, either by vaccination or by existing screening programs.

All good wishes and best regards.

Date : 24.2.2014

(Prof. Harald zur Hausen)
Prof Sukumar Mitra,
MBBS (Hons), Gold medalist,
MD, FRCOG (London)
Ex- Senior Gynecologist, SUN Hospital , Cuttack.
Ex-Prof. and Head, Department of Obstetrics and Gynecology SCB , Medical College Cuttack

Message

It is a pleasure to know that a group of pathologists, interested in cytopathology, have come forward to attend the problem of preventive aspect of cancer cervix and the younger generation of gynecologists have joined hands with their pathology counter parts.

In 1992 Parkin etal published comparative figures of several countries of the world about the probability of woman surviving the age of 75 developing cancer cervix. Three urban figures of India showed that among all countries, next to Brazil Indian women were most vulnerable to develop cancer cervix.

My interest in cancer cervix dated from student days in Patna (1940s) persisted during my training years in UK (1950s) where I had the opportunity to see the birth of cytology screening programme in a small laboratory in Post Graduate Medical School, London. The lone cytopathologist was Dr. Erica Wachtel.

Screening of cervical cancer, in fact of any cancer, is a part of National Health Programme, funded by Central and State Governments and implemented by interested cytopathologists and gynecologists. I was fortunate to be a life member of Association of cytopathologists of India 30 year ago, but unfortunately, I did not have opportunity of taking part in any screening programme. Central and State Governments were too busy with prevention of communicable diseases.

Cervical screening programme addresses the problem to find out the prevalence of the disease in various invasive stages in the population. More importantly it aims to find out
the prevalence of the disease in preinvasive stage which can be easily eradicated. Whether a premalignant disease, adequately treated, can again raise its head as a monster, in malignant from, in future, has to be established by long term follow up study. On this line some work has been done in the past.

So, can we dream a scene when cervical cancer in advanced stages will be nonexistent entity, early stage cervical cancer will be a freak in gynecological practice, perhaps due to imperfect screening providing false negative reporting and the mass of clinical material will be in premalignant stage. The evolution of normal epithelium in to premalignancy will be the matter for study in future. Theoretically, mortality from cervical cancer can be reduced to zero.

The biological behaviour along with the molecular interpretation of preinvasive cervical epithelium has to be subject of interest.

1. Can invasive malignancy occur de novo.
2. Elucidation of steps of transformation from preinvasive epithelium to invasive stage.
3. Can the process of transformation be hastened or delayed.
4. Can the preinvasive epithelium be static or regress.
5. Can the process of transformation recur after adequate treatment, the causative factor persisting.
6. The transformation process entirely of viral origin.
7. The cytological study of residual vaginal epithelium after Wertheim’s hysterectomy.

We are told that the meeting point of two embryonal epithelia is an unstable zone, the story of keeping peace at the line of control can be fascinating.

I wish the project of creating an awareness of cervical cancer, a first step in long journey, be a grand success. We can look forward to more and more women participate in the screening programme so that the scourge of the discuss will be a matter of past.

I whole heartedly commend your efforts.

Date: 6.3.2014

[Signature]

Prof. Sukumar Mitra
Cancer of the uterine cervix is a preventable lethal disease. Most of the patients present in advanced stages of the disease. HPV is known to be the necessary cause of the disease. Prevention can be achieved by health education, avoiding the risk factors and adopting screening strategies. Vaccination against high risk HPV will go in a long way to prevent the preventable disease.

I am glad to know that the ABC Foundation of Cuttack is contributing to a greater extent to organise such awareness programmes to educate public.

I wish all success in their endeavour.

Date: 25.02.2014

(Dr. S.K. Giri)
Dear Dr. Rout,

I am profoundly honored by your observing my birthday (March 11) as the “Cancer Cervix Eradication Day” at Cuttack, and I am very much impressed by your initiative to eradicate cervical cancer, which clearly still is a worldwide problem. I am sure that this initiative and the engagement of your crew are fulfilling a most important mission. Let me certainly warmly encourage you to continue the program of awareness for the prevention of cervical cancer, of public education, of active advocacy of public health officials and physicians. I wish this program a continued success.

All good wishes,

Date: 13.02.2015

Prof. Harald zur Hausen
Message

Dear Prof. Rout,

Thank you very much for your e-mail of Feb. 16. Due to a period of absence from Heidelberg I was unable to respond earlier. Certainly I am willing to send a message as follows:

I am honored by the observation of my birthday, March 11 as Cancer Cervix Eradication Day at Cuttack. I regret that I will be unable to participate in the event at your place. “The eradication of cervical cancer is clearly a global aim of substantial importance. With the availability of cytological tests, secondary prevention has been used for a long period of time and turned out to be quite successful in removing precursor lesions for subsequent cervical cancer development. Although this method developed by Georgios Papanikolaou has been clearly a major step forward, the recent availability of vaccines, up to now against human papillomavirus types 6, 11, 16 and 18 offered great additional possibilities. By now it is very clear that this vaccine is highly effective in preventing the lesions of the respective virus types in previously uninfected girls with a remarkable efficacy. Studies, in particular reported from Australia and also from the United States (New York Times: http://www.nytimes.com/2016/02/22/health/vaccine-has-sharply-reduced-hpv-in-teenage-girls-study-says.html?_r=0) show that this vaccination prevents precursor lesions and thus acts also in the prevention of surgical interventions. Although the presently available vaccines prevent between 70-80% of precursor lesions of cervical cancer, the future availability of vaccines containing nine different types will almost certainly bring this level to more than 90%.”

At the same time awareness is increasing that vaccination is also extremely important for boys. This is not only due to the fact that oropharyngeal cancers linked to the same types of papillomavirus infections occur in males at a relatively high frequency, but also due to the fact that males act in the transmission of this infection to their female partners. Fortunately, a number of countries by now started to develop vaccination programs for boys as well.

Let me congratulate you to your activities at Cuttack. It clearly will have a long-lasting effect in all those who receive the preventive measurements.

All good wishes and warm personal regards,

Date: 25.02.2016

(Prof. Harald zur Hausen)
Cancer Cervix Eradication Day Message

Dr. Lalatendu Sarangi, MS
Director,
Acharya Harihar Regional Cancer Centre
Cuttack-753007
Date: 23.02.2016

Message

Cancer of uterine cervix constitutes 20% of all cancers in women. In the last decade only, this was the commonest cancer of women & now slowly been taken over by breast cancer. This has been successful only because the awareness generated by socio-medical groups. Periodic PAP smear tests have contributed significantly along with the awareness. Vaccine against HPV is a definite boon against this cancer. So to spread the message on both these cancer prevention tools, PAP test & HPV Vaccine, a strong women centric movement is essential.

I am happy to learn the ABC foundation has taken a positive initiative in this path. They are observing 11th March as cancer cervix eradication day by CME, advertising through social media.

I wish their endeavour a great success.

(Dr. L. Sarangi)
F200, German Cancer Research centre (DKFZ)
Foundation Under Public Law
Im Neuenheimer Feld 280
69120 Heidelberg
Germany

Message

Dear Dr. Rout,

Thank you for your e-mail of March 2. Let me once again express my gratitude for declaring 11th March as "Cancer Cervix Eradication Day". I find your initiative encouraging and stimulating. I trust that these efforts of yourself and your colleagues will result in a higher degree of consciousness that cancer of the cervix is, indeed, one malignancy which has a reasonable chance to become eradicated. This will require continuous advocacy to implement the HPV vaccination not only for girls prior to reaching sexual maturity, but also for boys. The selected vaccination of females only will almost certainly delay the success of this vaccination program.

I wish you and your colleagues all the best, and certainly success in reaching as much of the eligible population as possible. I am very grateful for your tireless efforts.

With best regards,

Date: 6.3.2017

(Harald zur Hausen)
Message

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I wish their endeavour a great success.

Date: 23.02.2017

(Dr. L. Sarangi)
GLIMPSES OF CANCER CERVIX ERADICATION DAY
First Cancer Cervix Eradication Day: 2011

- Lighting Lamp by Prof. P.C. Mohapatra, President, FOGSI in presence of Prof. N.C. Parija, President, IAPM
- Release of Journal “Cancer Cervix Eradication” by Prof. Sukdev Nayak, Director, AHRCC, Cuttack
- Papanicolaou Samman bestowed on Prof. P.C. Mohapatra by Prof. B.K. Nanda
- abc Foundation Award presented to Dr. Bhagyalaxmi Nayak by Prof. G.S. Acharya

Respected members in the audience
Cancer Cervix Eradication Day: 2012

Dr. S.N Pradhan, Vice-President IAPM-2011, addressing the meeting

Dr. Asaranti Kar, Jt secretary IAPM (HQ) addressing the meeting

Dr. Bhagyalaxmi Nayak, Asst. Prof. Gynaecology, addressing the meeting

Dr. S.N Pradhan presenting ABC foundation Award to Dr. Pradyumna Kumar Sahoo

Members in the Audience

Prof. U.N Panda and Prof. Janardan Mohanty addressing the meeting
Cancer Cervix Eradication Day: 2013

Prof Badal Kumar Mohanty addressing after receiving Papanicolau Sammana

Prof Gyanendra Nath Mohanty delivering Dr. Harald zur Hausen Oration

Dr. Asamati Kar proposing vote of thanks

Prof. Badal Kumar Mohanty and Prof. N.C. Parija lighting the lamp

Group photo with Prof Gyanendra Nath Mohanty and Prof. Badal Kumar Mohanty

Cancer Cervix Eradication Day
11th March 2013
IAPM House
National Cancer Institute
Cuttack - 753014
Cancer Cervix Eradication Day : 2014

Prof B.K. Nanda and Prof N.C Panja felicitating Dr. Partha Basu of Kolkata

Prof Sukumar Mitra was felicitated with the Papanicolaou Sammanana

Prof. Susil Kumar Guha, Director AHRCC Cuttack releasing the souvenir

11th March 2014
IAPM HOUSE
CHAHATA, BIDANASI, CUTTACK - 753014

ABC Foundation Award was presented to Dr. Sanghamitra Pati by Prof. G.S. Acharya and Prof. N.C. Panja
Cancer Cervix Eradication Day: 2015

Prof B.K. Nanda and Prof N.C. Panja felicitating Prof Niraj Bhatia of AIIMS New Delhi. Prof Nirmal Bhatia delivered Dr. Harald zur Hausen Oration

The Papanicolaou Sammata was bestowed upon Prof Susil Kumar Giri

Group photo with Prof. Niraj Bhatia and Prof. Susil Kumar Giri
Cancer Cervix Eradication Day: 2017

Group photo with Prof Anita Maheswari

Audience

Audience

Prof Raghunari Mohanty releasing the souvenir

Prof N.C. Parja presenting ABC Foundation Award to Dr. Marisa Mohanty

Papanicolaou Sammna bestowed upon Prof Hemantha Swain by Prof G.N. Mohanty and Dr. Sarojini Panda

Prof B.K. Nanda felicitating Prof Anita Maheswari of TMH Mumbai

Prof Anita Maheswari delivered Dr. Harald zur Hausen Oration

Dr. Niranjan Rout, addressing the meeting
**Prof. Dr. Niranjan Rout** has passed MBBS (Hons) from Utkal University in the year 1979. He has completed his M.D from Utkal University in the field of Pathology. He has joined as Medical Officer, Health and FW Dept., Govt of Orissa in the year 1986. Later he worked as faculty in SCB medical college cuttack and finally now in A.H. Regional Cancer Center Cuttack since 1997. He has served the A.H. Regional Cancer Center Cuttack in various capacities and involved himself in many curricular and extra-curricular activities and working now as Dean and Principal. His research interest is in the area of Diagnostic Cytology, Oncopathology, Cervical Cancer, Molecular Biology, Microbiology. Two no. of Ph.D students and 3 no. of MD students have already awarded degree. He has published more than 60 number of research papers in national and international Journals of repute & presented more than 65 papers in many seminars, symposia, workshops and conferences. He has contributed chapters in IAPM Text Book of Pathology and co-author in Medical Laboratory Technology Book.

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