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A Study Of Human Papillomavirus (Hpv) Screening For Detection Of Cervical Cancer In Pregnancy And Postpartum

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Abstract:

Gynecological malignant tumours during pregnancy have increased in recent years, mostly due to an increase in the number of older women having pregnancies. Cervical cancer accounts for 71.6 percent of all pregnancy-related gynaecological malignancies, followed by ovarian malignancies at 7.0 percent. Cervical cancer in pregnant women is uncommon, and the symptoms are often mistaken for those of other illnesses. Misdiagnosis is more common during pregnancy since gynaecological examinations are restricted. Pregnancy-related cervical cancer treatment is dependent on a variety of variables, including tumour size and type, gestational length, lymph node involvement, and the willingness of the patient to carry the pregnancy to full term. Due of this, it is difficult to decide the best course of treatment. Cervical cancer in pregnancy can be diagnosed and treated effectively while protecting the fetus's health and avoiding delays in treatment and preterm births. This article highlights the latest research on the diagnosis and treatment principles of cervical cancer in pregnancy.

Keywords: cervical cancer, chemotherapy, diagnosis, pregnancy, pregnancy with cervical cancer, tumor management, tumor staging.

1. Introduction

Men and women around the world are susceptible to the human papillomavirus (HPV), which is estimated to be the most common sexually transmitted virus in the US. The incidence and prevalence of genital HPV infection remain unknown because it is not a condition that must be reported; however, it is estimated that between 1 million and 5.5 million new infections occur each year in the United States, and that the prevalence may be as high as 20 million. Rates of HPV infection appear to be increasing at an alarming rate, making the topic of HPV even more relevant.

Cases of cervical cancer that are diagnosed during pregnancy and six to 12 months after birth are included in this category of pregnancy complicated by cervical cancer. A very small number of women have pregnancies complicated by cervical cancer. Cervical cancer is diagnosed in about 1% to 3% of women who are pregnant or recently had a baby. The following are the first and second steps. Approximately half of these cases are diagnosed prenatally, while the other half are diagnosed within the first year of life. 3 At 0.8 to 1.5 occurrences per 10,000 babies, cervical cancer is one of pregnancy's most prevalent malignancies. Per every 100,000 women diagnosed with cervical cancer, there are four pregnancies compromised by the disease. The incidence of cervical cancer during pregnancy was found to be 0.016 percent (52/330 138) in data from 13 hospitals in China's 12 regions. Proving that cancer can be accelerated during pregnancy is still up in the air. Human papillomavirus (HPV) 16 and HPV 18 infection have been linked to higher levels of oestrogen,

progesterone, and human chorionic gonadotropin in pregnant women, which suggests that pregnancy may enhance cervical cancer growth. Pregnant women's increased lymphatic and blood flow to the reproductive organs, as well as their body's decreased immunity during the early stages of pregnancy and after delivery, among other things, may hasten tumour metastasis and hence raise their risk of cervical cancer.

Women between the ages of 20 and 35 are most at risk for HPV infection; nevertheless, the vast majority of these infections are asymptomatic and clear up on their own due to a strong immune system. Women are more sexually active than ever at this point in their lives. Pregnant women in this age range are particularly prevalent in poor countries. HPV infection may be more likely to remain during pregnancy because of the altered hormonal environment and immunological response.

Only about 0.004–0.1% of pregnant and postpartum women get cervical cancer (CCIP), a rare yet serious condition. As a result of population and screening programme disparities, the incidence of cervical cancer during pregnancy is expected to fluctuate. It is difficult to treat CCIP because of its rarity, and there are no randomised studies or major trials to draw from as a reference point. Thus, the existing guidelines for the management of CCIP are based on a small number of cases and expert opinions. CCIP treatment decisions should be made by multidisciplinary teams of gynecologic oncologists, obstetricians, pathologists, and neonatologists because both the mother and the foetus benefit from tailored care and psychological support throughout the pregnancy.

Although aggressive therapy for cervical cancer has gradually been replaced with more pregnancy-preserving management, particularly for patients in the second or third trimester of their pregnancies, CCIP treatment has evolved through time. Cervical cancer patients have been effectively treated with fertility-preserving alternatives such as radical or simple trachelectomy, with or without neoadjuvant chemotherapy (NACT). Early-stage cervical cancer may necessitate surgery as a main therapy option. It is an optional treatment for people with late stages of cervical cancer, which may delay the ultimate local treatment until term or after delivery.

Our study aimed to add to the clinical evidence by evaluating the clinical characteristics, management, and prognosis of cervical cancer in pregnant women of various gestational ages (GA) and comparing the subsequent outcomes of termination of pregnancy (TOP) and continuation of pregnancy (PT) given the limited data on maternal and foetal prognosis (i.e., PT vs. termination of pregnancy) (COP).

1.1 The Essential Virology

Papoviruses, which include polyomavirus and simian vacuolating virus, belong to the Papovaviridae family. HPV is a 55-nm-diameter virus that does not encase itself in an envelope. At least two capsid proteins—L1 and L2—are present in its icosahedral cap, which is made up of 72 capsomers. The main capsid protein L1 has five pentamers in each of the capsomers. L2 is a minor capsid protein that is found in roughly 12 copies per virion. When seen under an electron microscope, the virus is reported to resemble a golf ball. In all, the HPV genome contains roughly 7,900 base pairs (bp) of double-stranded, circular DNA linked to histones. ORF protein-coding sequences can only be found on one strand. Each of the three sections of the genome has a distinct purpose.

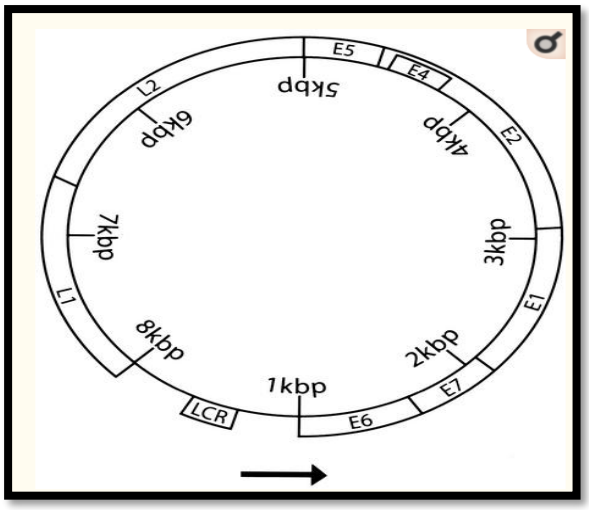

Figure 1.1 Schematic representation of the circular HPV DNA genome

One of the first is a 400 to 1,000 bp noncoding regulatory area that has been referred to as the noncoding region, long control regions (LCR), or higher regulatory regions. To regulate DNA replication, this region contains the p97 core promoter, as well as enhancer and silencer regions that modulate ORF transcription. The viral genome contains the most variety in this area. ORFs E1, E2, E4, E5, and E6, which are crucial in viral replication and oncogenesis, are found in the second region. This is the third and last region, which encodes the viral capsid's L1 and L2 structural proteins.

The nucleotide sequences of the E6, E7, and L1 ORFs of a new HPV type must not be more than 90% identical to the corresponding sequences of known HPV types [4-6]. Variants are those HPVs that show less than 98% sequence homology with their parent type, and subtypes are those that show 98% to 98% sequence homology with their parent type. Biological and metabolic features of several naturally occurring variations are crucial in cancer risk.

1.2 Assays for the Detection and Typing Of HPVs

Since HPV cannot be propagated in tissue culture, molecular biology techniques are typically used to accurately identify it. Nucleic acid probe technology is the preferred method for detecting HPV in clinical specimens because of its well-known physical structure and gene organisation. It is possible to directly detect the HPV genome and transcripts by using hybridization procedures such as Southern and Northern blottings, in situ hybridization, signal-amplification molecular technology (Hybrid Capture assay, version hc2; Digene; Gaithersburg, MD) and DNA sequencing . These assays can be made even more sensitive by the use of various signal detecting methods. This is the only method that may be able to identify all of the HPV types and variants in a biological specimen, either by cloning into plasmids or by direct sequencing of a polymerase chain reaction (PCR) fragment of the viral genome. However, the process is currently labor-intensive and expensive. More work needs to be done on the direct sequencing of specimens that include several HPV types. Solid phase hybridization for HPV genome analysis, such as Southern blot for DNA molecules and Northern blot for RNA molecules, are excellent procedures that can generate high-quality information, but they are time consuming and require large amounts of highly purified nucleic acids. They are, however, necessary. The hybridization in solid phase requires well-preserved, full-size molecules, and hence cannot be done with any biological specimen, particularly those generated from fixed tissues, in which DNA degradation is frequently seen. Large-scale population studies can't use this method since it's too time intensive and

difficult to implement. By using in-situ hybridization (ISH), specific nucleotide sequences in cells or tissue sections with preserved morphology can be recognised, making it possible to pinpoint exactly where the target genomes are located inside the biological object [8-12]. Because it may be used on tissues that have been routinely fixed and processed, ISH has a huge advantage over other techniques that have a lower analytical sensitivity limit. In-situ PCR, a technique that combines PCR with ISH to improve sensitivity [2], can be used to do this. When viral protein levels are low, ISH can be employed to identify messenger RNA (mRNA) as a gene expression marker [3]. Probe cross-hybridization introduces a significant risk of mistake in HPV typing. For HPV DNA and RNA detection in tissues, however, recent advancements have allowed it to become routinely employed.

1.3 Symptoms and Prevalence

Women worldwide are diagnosed with cervical cancer at a rate that is second only to breast cancer. Cervical cancer is one of the most frequently discovered tumours in pregnant women because it affects young women so regularly..

Now we know that HPV (human papillomavirus) plays an important role in cervical cancer development. Pregnant women are frequently diagnosed with preinvasive cytologic abnormalities due to the prevalence of HPV in young women. The vast majority of these changes are low-grade abnormalities that are generally temporary and resolve on their own. The risk of persistent high-grade abnormalities and, eventually, invasive cervical cancer in a reduced percentage of women.

Cervical cancer symptoms in pregnant women are linked to the tumor's clinical stage and diameter. It is rare for women who are pregnant with early-stage cervical cancer to experience any noticeable physical signs. In some cases, a patient's symptoms include vaginal discharge with smell, purulent or bloody secretions, and irregular bleeding from the vaginal canal. Pain from tumours or chronic anaemia from long-term irregular vaginal bleeding are the most common symptoms of pregnancy with late cervical cancer [10]. To avoid confusion, these patients are either pregnant or postpartum, which makes the above symptoms more likely to be misdiagnosed. Pregnant and postpartum women who experience vaginal bleeding should be closely monitored, and a gynaecological checkup and cervical exfoliation cytology screening should be performed if necessary.

1.4 The management scheme of pregnancy complicated with cervical cancer

Cervical cancer patients who want to preserve their fertility can undergo fertility-preserving surgery after terminating their pregnancy if they are in the stages I B1 or below of the disease, but if they are in the stages I B1 or below of the disease and their pregnancy is less than 20 weeks along, they should have a sexless abortion. Patients whose pregnancies are to be maintained should receive care tailored to their specific needs. Pregnancy can be maintained in women with stage I A1 cervical cancer who are fewer than 20 weeks pregnant, and therapy can begin after delivery. Stage I A1 cervical cancer in pregnancy had an invasive depth of less than 3 millimetres, according to Chinese researchers, and a lymph node metastatic rate of 0.6%. Cytology and colposcopy can be used to keep an eye on it. Postpartum treatment is an option if the malignancy has not progressed [11-13]. 24 Cervical conization has been suggested as a therapy option by several experts. Pathological diagnosis of cervical conization stage I A1 and positive incision margins need radical hysterectomy postpartum; if the incision margins are negative, total extrafascial hysterectomy should be performed postpartum. 11 In cases of stage IB or higher cervical carcinoma, NACT is indicated at 20 to 30 weeks of pregnancy to prevent complications. For this reason, paclitaxel (135-175 mg/m2)+cisplatin (70-75

mg/m2) once every three weeks after 20 weeks of gestation is currently used after 20 weeks of pregnancy and is relatively safe. 25 The development of the foetal lungs is accelerated after two to three rounds of chemotherapy. There was no significant difference in overall survival or progression-free survival between pregnant women receiving cisplatin and those receiving cisplatin alone, according to Song et al26. Cisplatin can be administered as a single drug therapy for pregnant women with cervical cancer in order to minimise the side effects of chemotherapy. After 35-37 weeks of pregnancy, a caesarean section can be performed to end the pregnancy, and cervical cancer can be treated with postpartum surgery, radiotherapy, and chemotherapy [14, 15]. NACT is utilised to maintain foetal maturation in cases of cervical cancer that are more than 30 weeks gestational age. Preventing bone marrow suppression (haemorrhage, infection, and anaemia) in mothers and infants, as well as the accumulation of cytotoxic medicines in newborns, can be accomplished with routine one-cycle chemotherapy and drug withdrawal three weeks prior to the expected due date.

2. Review of Literature

Nitish Beharee (2019), Gynecological malignant tumours during pregnancy have increased in recent years, mostly due to an increase in older women becoming pregnant. Cervical cancer accounts for 71.6 percent of all prenatal gynaecological malignancies, with ovarian malignancies accounting for the remaining 7.0 percent.There is a relatively low prevalence of cervical cancer in pregnancy, and the symptoms might be easily confused with those of other pregnancy-related illnesses. Misdiagnosis is more common during pregnancy since gynaecological examinations are restricted. There are various variables that affect the therapy of cervical cancer during pregnancy, including tumour size, pathological type [18], gestational age, lymph node involvement, and patient preference. Due to this, it is difficult to choose the best treatment. Cervical cancer in pregnancy can be diagnosed and treated effectively while protecting the fetus's health and avoiding delays in treatment and preterm delivery. This article highlights the current research advancements in this area.

Chung-Yuan Lee (2021). Women who have already gotten the human papillomavirus (HPV) vaccine need to have their vaccinations completed at a higher rate. When it comes to vaccines, a vaccination control programme and getting more women to finish their shots are essential, but they also pose enormous hurdles because they require repeated doses. When it comes to the background characteristics of postpartum women who are vaccinated or unprotected against HPV, there are currently no published studies. This study, which was based on a feasible HPV vaccination program, examined second and third-dose HPV vaccination rates in postpartum women. Between March and September of 2014, 243 postpartum mothers who visited Chiayi Chang Gung Memorial Hospital were included in this retrospective analysis [19]. In a practical, controlled postpartum HPVimmunisation programme, HPV vaccination was administered to some of these mothers, but not to others. Postpartum women's HPV vaccination rates for the second and third time were tallied. Students' t test, chi-square test, Fisher's exact test, and multivariate logistic models were used to determine the differences in background characteristics between the two groups. Ninety-seven percent of postpartum HPV vaccine recipients completed all three doses in a regulated vaccination regimen. Significant differences were found between the two groups in our study. These were according to the age of the mother, the gender of the newborn, and postpartum Pap smear results. The postpartum HPV vaccination programme is a feasible strategy to ensure that all three doses of postpartum vaccination are completed, and it might serve as a model for any multiple-dose vaccination procedure.

Shoichiro Ishii (2021) Prenatal uterine cancer screening in Japan is free because of government subsidies. During our study, we looked at the current status of the results of cervical cytology in Japan. Cervical cytology was requested from 2,293 obstetrical hospitals that delivered between October 2018 and March 2019. Overall, a total of 1,292 places of childbirth answered the call and provided useful details about 238,743 expectant mothers under their care. In Japan, 86.8% of pregnant women had their cervix cytology performed. It was shown that 3.3% of all pregnancies had abnormal cervical cytology, and 4.9% of them had abnormal cytology performed with a spatula/brush and liquid (LBC). Teenagers with atypical squamous cells of unknown significance (ASC-US) had a higher HPV positivity rate than women of other ages (p 0.01). Cervical cancer screening during pregnancy will need to be improved due to a lack of HPV vaccine uptake in Japan, which is now at less than 1%.

3. Materials and Method

Between January 2018 and January 2019, researchers at the All India Institute of Medical Sciences in Rishikesh's Department of Obstetrics and Gynecology conducted a prospective observational study. In the first 10 months of the trial, women were recruited, and they were followed up for six weeks postpartum. After receiving the go-ahead from the institutional review board and ethics committee, the investigation could finally get on in earnest. Pregnant women with BMI between 18 and 24.9 kg/m who consented to the study were included in the study, which included 237 women. A history of medical conditions such as hypertension, diabetes mellitus with vasculopathy, renal disease, and anti-phospholipid antibodies among pregnant women who are younger than 20 years old or older than 35 years old

Study participants were excluded from the study if they had a mother or paternal history of small for gestational age children or if they had a syndrome or chronic anaemia. After a thorough explanation of the study's scope, objective, and length in their native language, the couple gave their written and informed consent. As with non-pregnant patients, a Pap smear was conducted. When the procedure was complete, she was in the lithotomy position. Scraping from the cervix with Cusco's speculum allowed the cervix to be visualised

When photographing the squamo-columnar junction, a 360-degree swipe with an endocervical cytobrush and an ectocervical Ayres spatula was used [20]. It was then stained with Papanicolaou stain and examined by a pathologist after being placed evenly across the glass slide and promptly preserved with 95 percent alcohol for 30 minutes. After the surgery, the women were given advice and assurances about possible minor vaginal bleeding. Following the Bethesda method, results were expressed.

No intraepithelial lesion , atypical squamous cell of undetermined significance , ASC-H, squamous cell carcinoma, ASC-NOS, atypical glandular cells not otherwise specified , and adenocortical cells According to the American Society for Clinical Pathology , women who had abnormal cervical results were treated.

4. Results

Table 1: Distribution of Study Subjects on the basis of Demography

Basis	Group	No. of Cases	Percentage %
Age (years)	20-25	102	43

	26-30	94	39
	31-35	41	18
Parity	Multipara	139	58
	Primipara	98	42
POG (Weeks)	<14	71	30
	14 to 28	128	54
	>28	38	16
Education level	Primary	26	11
	Secondary	44	18.50
	High school (matric)	39	16.50
	Intermediate (+2)	89	37.50
	Graduate	39	16.50
Socio economic status	Lower	93	39
	Lower middle	125	53
	Upper middle	19	8

Table 1. shows the socio demographic of the patients age, parity , educationa level and socio economic status

Table 2: Distribution of P/S Findings

Per speculum finding	No.of case (s)	Percentage %
Circumoral Erosion Present & Bleeding On Touch	1	0.55
Circumoral Erosion & Nabothian Cyst Present	1	0.55
Circumoral Erosion Present &Cx Hypertrophied	2	0.80
Thick Mucoid Discharge Present	3	1.20
Circumoral Erosion Present	6	2.50

Thick Curdy Discharge Present	7	2.90
Cx& Vagina Healthy	217	91.50
Total	237	100

Table 2 shows the per-speculum examination it was determined that 217 out of 237 pregnant women (91.5%) had normal cervix and vagina.

Table 3: Antenatal V/s Postnatal Pap Smear Results

Cross tabulation		Progression	Regression	Unchanged	Total	P-Value
Antenatal pap smear findings	NILM	0	0	193	193	<0.01
	ASCUS	0	4	0	4	
	ASC-H	0	1	0	1	
	HSIL	0	0	1	1	
	AGC	0	1	0	1	
	Total	0	6	194	200	

Table 3. shows the postnatal Pap smear screening test for the seven women who tested positive for premalignant lesions of the cervix . Four cases of ASCUS, one case of AGC, and one case of ASCH regressed, testing as NILM.

After screening 630 women, 237 women met the eligibility requirements and completed pap smear testing.' Between the ages of 20 and 35, these women conceived naturally, with a mean age of 26.63.8 years . Small for gestational age was not a concern in any of these women. An 85.7 percent regression rate was found, with a persistence rate of 14.2 percent for high-grade lesions (AGC and ASC-H) and a 57.1 percent regression rate for low-grade lesions (ASCUS). Several more studies have been conducted around the world to examine the postpartum regression rate of cervix lesions of low and high grade. The Pap smear results of 229 of the 237 prenatal women (96.6 percent) were negative for Intraepithelial Lesions or Malignancy (NILM). Antenatal Pap smear results revealed pre-malignant cervix lesions in 34% of women tested positive for prenatal cancers. One or more additional abnormalities were found in 25.7% of the 237 women undergoing prenatal care.

5. Conclusions

Atypical, readily confused with other pregnancy disorders, easily masked by the fact that one is pregnant, and difficult to detect are the signs and symptoms of a pregnancies affected by cervical cancer. According to their findings, spontaneous preterm delivery was not connected with BV, although LBW and SGA were. HPV vaccination and regular screening of pregnant women is critical to preventing cervical cancer and ensuring the health of their unborn children. It's impossible to overstate how critical it is to raise awareness about the

Pap smear screening test in India. As a part of this study, we took advantage of antenatal visits to screen for cervical cancer. Only one case of miscarriage was found to have ASC-H in the antenatal Pap smear test, and this was the only one we could find. preference for a possible pregnancy interference by the high-grade lesion

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