ORIGINAL RESEARCH

Evaluation of pre-invasive lesions associated with cervical carcinoma using a variety of screening methods- A comparative study

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ABSTRACT
Background: Cancer screening is simple and may be performed in pre-invasive phases, allowing for conservative and effective care of these lesions by chemoradiotherapy or surgery. The purpose of the current study was to examine the various techniques for identifying and screening cervical cancer pre-invasive lesions, including colposcopy, pap smear, visual cervix examination with iodine and acetic acid, and visual cervix examination with Lugol's iodine. **Materials and Procedures:** Following the taking of a medical history, 80 females between the ages of 20 and 60 had a colposcope, pap smear, acetic acid, and Lugol's iodine cervix examination. The statistical analysis of the acquired data was performed, and the findings were developed using a significance level of 0.05. **Results:** Only 2.5% (n=2) subjects had cervix with no abnormality, whereas 56.25% (n=45) females had cervicitis, 22.5% (n=18) subjects had Intraepithelial carcinoma-1, 16.25% (n=13) had Intraepithelial carcinoma-2/3, and 2 (2.5%) subjects had confirmed Micro invasive carcinoma using Lugol's iodine and acetic acid with a visual examination, pap smear, and colposcopy. **Conclusion:** According to the study, using pap smear cytology, visual inspection, and colposcopy together increases the likelihood of finding pre-invasive and invasive lesions.
Keywords: Cervical carcinoma, carcinoma cervix, pap smear, colposcopy

INTRODUCTION

Cervical cancer is a rising medical condition that affects people all over the world, although it is more common in poorer nations (around 88%) because of their poor access to healthcare. The second most common cause of mortality for women worldwide is cervical cancer, with most cases being recorded in Asia. The highest rates of cervical cancer in the world are seen in Aizwal and Thiruvananthapuram, where 8.8 and 22.5/1000 females, respectively, have the disease. This places a heavy load on this patients.[1]

Due to the lengthy pre-invasive period, where cervical carcinoma underwent a series of events before progressing to an invasive state, including cellular atypia, dysplasia, and/or intraepithelial neoplasia (CIN), invasive cervical carcinoma is considered a preventable entity.

Cervical cancer screening is simple and may be performed in pre-invasive phases, enabling conservative and effective care of these lesions by chemoradiotherapy or surgery. An ideal screening technique should be affordable, barely intrusive, simple to use, effective, and acceptable.[2]

There are several ways to screen for precancerous lesions and cervical cancer, including the gold-standard Pap cytology smear. Due to technological restrictions, which can enable early identification and screening effectiveness in high-risk females, its usage is nonetheless restricted.[3] Abnormal Pap smears are a marker of early neoplastic alterations, and CIN 2 and 3 have sensitivity ranges of 47 to 62% and 60 to 95 percent, respectively.

Due to a few flaws in the PAP smear, such as errors in sample, fixation, and interpretation, it is possible to

miss instances even though it catches roughly 30% of newly reported cases each year. India is home to 16% of all cases worldwide, just 5% of which are early-stage detections. Another method for early diagnosis and referral of malignant and premalignant lesions to higher centres for therapy and education of females about the course of the illness, symptoms, prophylaxis, and risk factors is known as downstaging.[4]

Colposcopic examination using a Colposcope is an additional examination technique for evaluating the lower genital tract to accurately distinguish between normal (benign) and abnormal to suspect pre-invasive and invasive abnormalities. Colposcopy is preferred over cytology and Pap smear because it is non-invasive, aids in locating the best locations for biopsies, and is the gold standard.

Due to a lack of resources, information, understanding, psychological factors, and a lack of responsiveness to screening, Indian females continue to be unaware of cervical cancer, related symptoms, and dangers. The chance that a female will get screening depends on her level of knowledge on cervical cancer.[5] In order to examine the various approaches for identifying and screening pre-invasive lesions of cervical cancer, including colposcopy, visual cervix examination with Lugol's iodine, visual cervix examination with acetic acid, and pap smear, the current trial was conducted.

MATERIALS AND METHODS

The institution's Department of Obstetrics and Gynecology conducted the current cross-sectional investigation. Based on inclusion and exclusion criteria, the study comprised 80 females with a mean age of 32.6 years who were in the 20–60 age range.

Females 18 years of age or older who visited an institutional OPD, subjects without any other systemic disorders, individuals not taking long-term medicine, subjects who consented to participate, and subjects who were willing to be followed up were the inclusion criteria for the study. Participants with ages between 20 and 60, pregnant women, history of hysterectomy, refusal to participate, proven aggressive cancer, and participants without a history of sexual activity in their lives were excluded from the study.

The institution's Department of Obstetrics and Gynecology conducted the current cross-sectional investigation. Based on inclusion and exclusion criteria, the study comprised 80 females with a mean age of 32.6 years who were in the 20–60 age range.

Females who were sexually active either now or in the past were selected, and after gaining consent, the reason for screening was presented. The test findings were then examined with the individuals, and if necessary, treatment information was provided. After patients were included, obstetric and menstrual histories were recorded along with any prior cervix surgery. After taking their medical histories, the individuals were placed in the dorsal position, and a speculum was inserted without lubrication to look for any pathology.

After applying 5% acetic acid for 60 seconds, acetowhite regions were examined visually to determine their boundaries, opacity, and thickness. Following the application of Lugol's iodine, an inspection was conducted to check for any color changes after 60 seconds. In a healthy cervix, the squamous epithelium becomes black or mahogany brown with no alteration to the columnar epithelium. The scarping squamocolumnar junction and posterior fornix were used to obtain pap smears after visual inspection with an ayre's spatula. These samples were subsequently mounted on slides using ether and ethyl alcohol. The smears were pathologically examined, and utilizing the updated Bethesda approach, conclusions were drawn. The Lugol's iodine, acetic acid, green filter, and regular saline were used during the colposcopic examination.

Modified Reid Colposcopic Index (RCI) was used for results prediction which is used for reference signs including margin, iodine response, vascular pattern, and margins where each component is scored from 0-2. The scoring system is as follows:

Scores of 0-2: low-grade disease (CIN1 or HPV)
Scores of 3-4: intermediate grade disease (CIN1 – II)
Scores of 5-8: high-grade disease (CIN II-III).

The collected data were subjected to the statistical evaluation using SPSS software version 21.0, 2012, Armonk, NY and the results were formulated keeping the level of significance at $p < 0.05$.

RESULTS

The study included 80 females were within the age group of 20-60 years of age with a mean age of 32.6 years. The other demographic and obstetric characteristics of the study subjects are described in Table 1.

The age group of 31–40 years had the highest percentage of female research participants—38.75% (n=31), followed by 41–50 years with 27.5% (n=22), and the age group of 51–60 years had the lowest percentage of participants—12.5% (n=10). All of the participants had parity of two (35%, n=28) or more (65%, n=52) in terms of parity. Abdominal tubectomy, Laparoscopic tubectomy, Copper-T, and oral contraceptives were the family planning techniques utilized by research participants in relative amounts of 46.25% (n=37), 11.25% (n=9), 7.5% (n=6), and 1.25% (n=1), whilst 33.75% (n=27) of the females did not use any kind of contraception. White discharge was the most common complaint among research participants who were female (n=66), followed by uterine bleeding (11.25%; n=9), post-menopausal hemorrhage (3.75%; n=3), and post-coital bleeding (2.5%).

A visual inspection using Lugol's iodine and acetic acid revealed that 47.5% (n=38) and 48.75% (n=39) of females, respectively, gave positive findings, according to the various screening techniques used in

the current study. Colposcopy outcomes were seen to be normal, erosion/inflammation, CIN 1, CIN 2/3, and unsatisfactory in 7.5% (n=6), 51.25% (n=41), 13.75% (n=1), 21.25% (n=17), and 6.25% (n=5) of individuals, respectively. Results of the Pap test revealed squamous metaplasia, Negative for intraepithelial lesion, and Negative for intraepithelial lesion. Inflammatory, low grade, high grade, and atypical squamous cells of unknown significance were found in 3.75% (n=3), 2.5% (n=2), 72.5% (n=58), 6.25% (n=5), 11.25% (n=9), and 1.25% (n=1) study females, respectively. Squamous cell carcinoma was found in 2.5% (n=2) subjects.

As demonstrated in Table 2, Pap smear results for research participants revealed inflammatory lesions, squamous metaplasia, candida species, bacterial vaginosis, and/or trichomonas vaginalis.

In terms of overall diagnosis and screening (Table 3), it was observed that 2.5% (n=2) of subjects had a cervix that was free of abnormalities, whereas 56.25% (n=45) of female subjects had cervicitis, 22.5% (n=18) of subjects had intraepithelial carcinoma-1, 16.25% (n=13) of subjects had intraepithelial carcinoma-2/3, and 2 (2.5%) of subjects had confirmed Micro invasive carcinoma. The findings of the current study's examination of the diagnostic accuracy of various screening techniques are presented in Table 4, where a comparative analysis was performed and it was discovered that 15 of the 32 cases of colposcopy positivity that were not detected by a pap smear.

Additionally, out of 48 negative colposcopic cases, 10 instances could not be identified by pap smear, demonstrating that they were able to identify false-positive and false-negative findings. In the ocular Lugol's iodine examination, 5 cases out of 48 negative cases and 11 cases out of 32 positive cases were missed.

Characteristics	Subgroup	%	N
Age range	20-30 years	21.25	17
	31-40 years	38.75	31
	41-50 years	27.5	22
	51-60 years	12.5	10
	Mean Age		32.6
Parity	Nullipara	0	0
	1	0	0
	2	35	28
	More than 2	65	52
Methods of family planning	None	33.75	27
	Abdominal tubectomy	46.25	37
	Oral contraceptives	1.25	1
	Laparoscopic tubectomy	11.25	9
Chief complaint	Post-menopausal bleeding	2.5	2
	White discharge	82.5	66
	Uterine bleeding	11.25	9
	Post-coital bleeding	3.75	3

Table 1: Demographic and Obstetrics characteristics of the study subjects

Screening methods	Subgroup	Lugol's Iodine Positive	Lugol's Iodine Negative	Acetic acid positive	Acetic acid Negative
Visual Examination	Normal	0	2	0	2
	Cervicitis	5	39	5	39
	Intraepithelial carcinoma-1	18	0	18	0
	Intraepithelial carcinoma-2/3	13	1	14	0
	Micro invasive carcinoma	2	0	2	0
	Total	38 (47.5)	42 (52.5)	39 (48.75)	41 (51.25)
Pap smear		**%**		**N**	
	Negative for intraepithelial lesion	3.75		3	
	Negative for intraepithelial lesion, squamous metaplasia	2.5		2	
	Inflammatory	72.5		58	
	low-grade squamous intraepithelial lesion	6.25		5	
	high-grade squamous intraepithelial lesion	11.25		9	
	atypical squamous cells of	1.25		1	

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	undetermined significance		
	Squamous cell carcinoma	2.5	2
Colposcopy	Normal	7.5	6
	Erosion/Inflammation	51.25	41
	Hazy acetowhite areas, fine punctations or mosaicism, iodine partial positivity (CIN 1)	13.75	11
	Dense acetowhite areas, coarse punctations or mosaicism, iodine negative epithelium (CIN 2/3)	21.25	17
	Unsatisfactory	6.25	5

Table 2: Screening methods employed in study subjects

Characteristics	N	%
Normal	2	2.5
Cervicitis	45	56.25
Intraepithelial carcinoma-1	18	22.5
Intraepithelial carcinoma-2/3	13	16.25
Micro invasive carcinoma	2	2.5

Table 3: Distribution of Pre-invasive and invasive lesions in study subjects

Parameter	Subgroup	N	Colposcopy	
			Positive	**Negative**
Pap	Negative	54	15	38
	Positive	26	17	10
Visual Lugol's iodine	Negative	42	4	38
	Positive	38	28	10
Visual acetic acid	Negative	41	5	37
	Positive	39	27	11

Table 4: Diagnostic efficacy of various screening methods employed in the study

DISCUSSION

In the current study, the age groups with the highest percentage of female participants were 31–40 years old (n=31), followed by 41–50 years old (n=22), and the age groups with the lowest percentage of participants were 51–60 years old (n=10). All of the participants had parity of two (35%, n=28) or more (65%, n=52) in terms of parity.

Abdominal tubectomy, Laparoscopic tubectomy, Copper-T, and oral contraceptives were the family planning techniques utilized by research participants in relative amounts of 46.25% (n=37), 11.25% (n=9), 7.5% (n=6), and 1.25% (n=1), whilst 33.75% (n=27) of the females did not use any kind of contraception. White discharge was the most common complaint among research participants who were female (n=66), followed by uterine bleeding (11.25%; n=9), post-menopausal hemorrhage (3.75%; n=3), and post-coital bleeding (2.5%). These results were comparable to those of Mehta A et al[6] in 2013 and Geethalakshmi U et al[7] in 2014, who found that the research patients had similar obstetric and demographic characteristics. 47.5% (n=38) and 48.75% (n=39) of the females who underwent visual examination using Lugol's iodine and acetic acid, respectively, exhibited positive findings. Colposcopy outcomes were seen to be normal, erosion/inflammation, CIN 1, CIN 2/3, and unsatisfactory in 7.5% (n=6), 51.25% (n=41), 13.75%

(n=1), 21.25% (n=17), and 6.25% (n=5) of individuals, respectively. Inflammatory, low grade, high grade, and atypical squamous cells of undetermined significance were found in 3.75% (n=3), 2.5% (n=2), 72.5% (n=58), 6.25% (n=5), 11.25% (n=9), and 1.25% (n=1) study females, respectively. Squamous cell carcinoma was found in 2.5% (n=2) subjects. These findings were in agreement with Ghosh P et al[8] in 2012 for a pap smear, Garg P et al[9] in 2011 for acetic acid and Lugol's Iodine, and Richa D et al[10] in 2014 concerning the colposcopic examination.

It was shown that only 2.5% (n=2) subjects had cervix with no abnormality, whereas 56.25% (n=45) females had cervicitis, 22.5% (n=18) subjects had Intraepithelial carcinoma-1, 16.25% (n=13) had Intraepithelial carcinoma-2/3, and 2 (2.5%) subjects had confirmed Micro invasive carcinoma. Awasthy S et al[11] in 2012 also showed a similar prevalence of these lesions in their subjects.

Regarding the diagnostic effectiveness of different screening methods, the findings are given in Table 4, where a comparative analysis was conducted and it was discovered that 15 of the 32 positive cases by colposcopy that were not found by a pap smear. Additionally, out of 48 instances with negative colposcopic results, 10 cases were misdiagnosed by pap smear, demonstrating that they were able to detect

false-positive and false-negative results. In the ocular Lugol's iodine test, 5 out of 48 negative cases and 11 out of 32 positive cases remained unnoticed. The investigations by Kushtagi P et al[12] in 2002 and Gopal M et al[13] in 2013 that demonstrated comparable diagnostic effectiveness of various screening approaches were supplemented by our findings.

CONCLUSION

Within its constraints, the current study draws the conclusion that when used together, pap smear cytology, visual inspection, and colposcopy have a better detection probability of pre-invasive and invasive lesion than when used alone. White discharge was the most often reported presenting complaint. Multiparous females had a significant incidence of intraepithelial cancer. Therefore, these procedures should be used in the normal cervical examination to identify and treat pre-invasive lesions early on, before they develop into cancer. The study did, however, have a few drawbacks, including geographic region bias, a small sample size, a cross-sectional design, and a brief observation time. To draw a firm conclusion, further longitudinal studies with a longer monitoring time and a bigger sample size are needed.

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