Comparative Evaluation of Various Screening Methods for Detecting Pre-invasive Lesions Associated with Carcinoma of The Cervix

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Abstract

Background: Owing to the easy examination accessibility of the cervix, cancer screening is easy and can be done in pre-invasive stages allowing conservative and successful management of these lesions by chemoradiotherapy or surgery**. Aims:** The present trial was carried out to compare various methods available for detecting and screening the pre-invasive lesions of cervical carcinoma including visual cervix examination using Lugol's iodine, visual cervix examination using acetic acid, colposcopy, and pap smear. **Materials and Methods:** In 80 females of 20-60 years,following history recording, the cervix examination was performed with acetic acid, Lugol's iodine, colposcope, and pap smear. The collected data were subjected to the statistical evaluation and the results were formulated keeping level of significance at p<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:** The study concludes that pap smear cytology, visual examination, and colposcopy used collectively has higher detection probability of pre-invasive and invasive lesion compared to when used individually.
Keywords: Cervical carcinoma, carcinoma cervix, pap smear, colposcopy, pre-invasive cervical lesions.

Introduction

Cervical carcinoma is a growing healthcare ailment prevalent globally, but affecting developing countries (approximately 88%) more, especially with limited healthcare resources. Carcinoma cervix is the second leading cause of female death globally with a major proportion of deaths reported in Asia alone. Indians constitute every fifth female having cervical carcinoma in World, imposing a great burden on these patients with the highest cases in Aizwal and Thiruvananthapuram with 8.8 and 22.5/1000 females respectively having carcinoma cervix [1].

Invasive cervical carcinoma is considered a preventable entity owing to its long course in the pre-invasive period, where on microscopic evaluation, before progressing to invasive state, cervical carcinoma undergoes a series of events from cellular atypia to dysplasia, and/or intraepithelial neoplasia (CIN). Owing to the easy examination accessibility of the cervix, cancer screening is easy and can be done in pre-invasive stages allowing conservative and successful management of these lesions by chemoradiotherapy or surgery. An ideal screening method should be cost-effective, minimally invasive, easily performed, have efficacy, and acceptable [2].

Screening of cervical cancer and precancerous lesions can be done by various methods including Pap cytology smear considered gold-standard.

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However, its use is limited owing to technical limitations, encompassing which can allow early detection and screening quality in high-risk females [3].Abnormal Pap smear signifies early neoplastic changes with sensitivity in CIN 2 and 3 of 47-62% and 60-95%respectively. Case detection can be missed with pap smear which detects nearly 30% of cases added every year owing to its few shortcomings like the error in sampling, fixation, and interpretation.A total of the world's 16% cases are recorded in India with only 5% detected in the early stage.

Downstaging is another technique used for early detection and referral of malignant and premalignant lesions to higher centers for management and education of females for disease progression, symptoms, prophylaxis, and risk factors [4].

Colposcopic examination using Colposcope is another examination method of assessing the lower genital tract to differentiate normal (benign) from abnormal to suspect pre-invasive and invasive lesions with high accuracy. Colposcopy is considered superior to cytology and Pap smear, non-invasive, helps to determine biopsy sites and needs and is considered gold-standard. Indian females remain ignorant about cervical cancer, associated symptoms, and risks owing to lack of resources, knowledge, psychology, and no response to screening. Knowledge about cervical cancer is a necessary factor in determining the likelihood of whether a female will undergo screening or not [5]. Hence, the present trial was carried out to compare various methods available for detecting and screening the pre-invasive lesions of cervical carcinoma including visual cervix examination using Lugol's iodine, visual cervix examination using acetic acid, colposcopy, and pap smear.

Materials and methods

The present cross-sectional study was carried out at Department of Obstetrics and Gynaecology, GSL medical college, Rajamundary,

Andhra Pradeshafter obtaining the approval from the concerned Ethical committee. The study included 80 females were within the age group of 20-60 years of age with the mean age of 32.6 years based on inclusion and exclusion criteria.

The inclusion criteria for the study were females of age 18 years or more visiting institutional OPD, subjects with no other systemic diseases, subjects not on prolonged medication, subjects consenting to participate, and subjects willing for follow-up. The exclusion criteria were subjects younger to 20 years and elder to 60 years, pregnant females, history of hysterectomy, non-willing to participate, confirmed invasive carcinoma, and subjects with no history of sexual intercourse ever in their life.

Sexually active females presently or previously in their life were identified and after obtaining consent were explained about screening needs. The subjects were then reviewed with the test results and were explained about treatment if required. After the inclusion of subjects, any previous surgery on the cervix was noted along with obstetric and menstrual history. Following history recording, the cervix examination was performed with subjects in dorsal position, and after inserting speculum without lubricants to identify any pathology on visualization.

For visual examination, after 60 seconds of 5% acetic acid application, acetowhite areas were evaluated concerning borders, opacity, and thickness. Concerning Lugol's iodine application, the examination was done after 60 seconds for detection of color change.No change in the columnar epithelium and squamous epithelium turns black/mahogany brown in the normal cervix. Following examination visually, with ayre's spatula, a pap smear was collected by the scarping squamocolumnar junction and posterior fornix, which were then fixed on slides using ether and ethyl alcohol. The smears were pathologically analyzed, and results were formulated using the revised Bethesda system. The colposcopic examination was done using Lugol's iodine, acetic acid, green filter, and normal saline.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.

Table 1: Demographic and Obstetrics characteristics of the study subjects

Characteristics	Percentage (%)	Number (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
Copper-T	7.5	6
Chief complaint		
Post-menopausal bleeding	2.5	2
White discharge	82.5	66
Uterine bleeding	11.25	9
Post-coital bleeding	3.75	3

The maximum study females were within the age group of 31-40 years having 38.75% (n=31), followed by 41-50 years with 27.5% (n=22), and least subjects were in the age group of 51-60 years with 12.5% (n=10) subjects. Concerning parity, all subjects had parity of 2 (35%, n=28) or more (65%, n=52). The family planning methods used by study subjects were abdominal tubectomy, Laparoscopic tubectomy, Copper-T, and Oral contraceptives in 46.25% (n=37), 11.25% (n=9), 7.5% (n=6), and 1.25% (n=1) subjects respectively, whereas 33.75% (n=27) females did not use any contraceptive method.The chief complaint reported by study females were white discharge by 82.5% (n=66) subjects, followed by uterine bleeding in 11.25% (n=9), post-menopausal bleeding in 3.75% (n=3), and post-coital bleeding in 2.5% (n=2) subjects.

Various screening methods assessed in the present study showed that visual examination using Lugol's iodine and acetic acid showed 47.5% (n=38) and 48.75% (n=39) females respectively showed positive results. Concerning colposcopy, it was seen that normal, erosion/inflammation, CIN 1, CIN 2/3, and unsatisfactory results were respectively shown in 7.5% (n=6), 51.25% (n=41), 13.75% (n=1), 21.25% (n=17), and 6.25% (n=5) subjects. Pap smear results showed Negative for intraepithelial lesion, Negative for intraepithelial lesion, squamous metaplasia, Inflammatory, low grade squamous intraepithelial lesion, high grade squamous intraepithelial lesion, and atypical squamous cells of undetermined significance were seen 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, whereas, squamous cell carcinoma was seen in 2.5% (n=2) subjects.Pap smear showed inflammatory lesions, squamous metaplasia, candida species, bacterial vaginosis, and/or trichomonas vaginalis in study subjects as shown in Table 2.

Table 2: Screening methods employed in study subjects

Screening methods				
Visual Examination	Lugol's Iodine Positive	Lugol's Iodin Negative	Aceticacid positie	Aceticacid Negative
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	Percentage (%)		Number (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 undetermined significance	1.25		1	
Squamous cell carcinoma	2.5		2	
Colposcopy	Percentage (%)		Number (n)	
Normal	7.5		6	
Erosion/Inflammation	51.25		41	
Hazy acetowhite areas, fine punctations or mosaicism, iodinepartial 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	

Concerning overall diagnosis and screening (Table 3),

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

Characteristics	Percentage (%)	Number (n)
Normal	2.5	2
Cervicitis	56.25	45
Intraepithelial carcinoma-1	22.5	18
Intraepithelial carcinoma-2/3	16.25	13
Micro invasive carcinoma	2.5	2

it was seen 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.

The present study also assessed the diagnostic efficacy of various screening tests evaluated and the results are described in Table 4 where the comparative evaluation was done and it was seen that out of 32 positive cases by colposcopy, 15 were not diagnosed by a pap smear. Also, among 48 negative colposcopic cases, 10 cases were not diagnosed by pap smear showing they detected false-positive and false-negative results. For visual Lugol's iodine examination, among 48 negative cases, 5 cases went undetected, and among 32 positive cases, 11 went undetected.

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

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

Discussion

In the present study,maximum females were within the age group of 31-40 years having 38.75% (n=31), followed by 41-50 years with 27.5% (n=22), and least subjects were in the age group of 51-60 years with 12.5% (n=10) subjects. Concerning parity, all subjects had parity of 2 (35%, n=28) or more (65%, n=52). The family planning methods used by study subjects were abdominal tubectomy, Laparoscopic tubectomy, Copper-T, and Oral contraceptives in 46.25% (n=37), 11.25% (n=9), 7.5% (n=6), and 1.25% (n=1) subjects respectively, whereas 33.75% (n=27) females did not use any contraceptive

method. The chief complaint reported by study females were white discharge by 82.5% (n=66) subjects, followed by uterine bleeding in 11.25% (n=9), post-menopausal bleeding in 3.75% (n=3), and post-coital bleeding in 2.5% (n=2) subjects. These findings were comparable to the findings of Mehta A et al[6] in 2013 and Geethalakshmi U et al [7]. in 2014 where comparable demographic and obstetric characteristics were seen in study subjects.

Visual examination using Lugol's iodine and acetic acid showed 47.5% (n=38) and 48.75% (n=39) females respectively showed positive results. Concerning colposcopy, it was seen that normal, erosion/inflammation, CIN 1, CIN 2/3, and unsatisfactory results were respectively shown in 7.5% (n=6), 51.25% (n=41), 13.75% (n=1), 21.25% (n=17), and 6.25% (n=5) subjects. Pap smear results showed Negative for intraepithelial lesion, Negative for intraepithelial lesion, squamous metaplasia, Inflammatory, low grade squamous intraepithelial lesion, high grade squamous intraepithelial lesion, and atypical squamous cells of undetermined significance were seen 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, whereas, squamous cell carcinoma was seen 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.

Concerning diagnostic efficacy of various screening tests evaluated and the results are described in Table 4 where the comparative evaluation was done and it was seen that out of 32 positive cases by colposcopy, 15 were not diagnosed by a pap smear. Also, among 48 negative colposcopic cases, 10 cases were not diagnosed by pap smear showing they detected false-positive and false-negative results. For visual Lugol's iodine examination, among 48 negative cases, 5 cases went undetected, and among 32 positive cases, 11 went undetected. These findings complemented with the studies of Kushtagi P et al [12]. in 2002 and Gopal M et al [13]. in 2013 where similar diagnostic efficacy of these screening methods was reported.

Conclusion

Within its limitations, the present study concludes that pap smear cytology, visual examination, and colposcopy used collectively has a higher detection probability of pre-invasive and invasive lesion compared to when used individually. The most common presenting complaint was white discharge. A high incidence of intraepithelial carcinoma was seen in multiparous females. Hence, these methods should be administered in the routine cervical examination for early detection and management of pre-invasive lesions before their progression to carcinoma. However, the study had few limitations including geographical area bias, small sample size, cross-sectional nature, and short monitoring period. Hence, more longitudinal studies with a long monitoring period and larger sample size are required to reach a definitive conclusion.

Conflict of Interest: Nil Source of support: Nil

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