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ORIGINAL ARTICLE

Clinical Scoring System to Detect Malignant and Premalignant Vulval Lesions

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Abstract
Objective To construct a simple clinical scoring system for evaluation of vulval lesions that will be helpful in clinically detecting the premalignant or malignant lesions of vulva.
Methods Seventy women referred for vulval examination at a tertiary care centre in north India were examined over a period of 2 years. Biopsy was performed in 66 consenting women. Association of high-grade vulval lesion with various clinical parameters such as age, duration of symptoms, presenting complaints, the presence of depigmentation, ulceration, hyperkeratosis, acetowhite changes on acetic acid application, asymmetrical distribution of the lesion, surface elevation on naked eye or colposcopy, induration on palpation and toluidine blue stain retention was studied. The significantly associated factors were assigned a value of 0 or 1 depending on whether they were present or absent. Score was then formulated for detection of high-grade lesion defined as moderate to severe dysplasia and early malignancy.
Main outcome measures Histopathology.
Results Out of the various parameters that were studied, duration of symptoms more than 6 months, hyperkeratosis, asymmetrical distribution of the lesion, surface elevation on naked eye or colposcopy, induration on palpation and positive toluidine blue stain retention of the lesion were found to be significantly associated with a malignant or premalignant lesion. It was found that a score of equal to or greater than 3/6 was significantly associated with a malignant or premalignant lesion.
Conclusion This simple scoring system has a potential to identify the high-grade lesions and can be used to identify the vulval lesion requiring a biopsy or further referral to higher centre.

Keywords Vulva · Preneoplastic lesion · Malignancy · Score

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Introduction

Identification of lesion at high risk of malignant or premalignant change is priority in women presenting with any vulval lesion. In women with chronic non-neoplastic epithelial disorders such as lichen sclerosus, squamous hyperplasia and mild Vulvar Intraepithelial Neoplasia (VIN) there is a need for long-term monitoring for development of malignant or premalignant changes as 3–6 % of patients with lichen sclerosus will develop invasive vulval carcinomas [1]. Role of colposcopy and colorimetric tests—acetic acid and toluidine blue test, used as isolated tests in the diagnosis of vulvar disorders, has been questioned [2]. Utilization of

multidisciplinary approach has been suggested for management of vulval lesions suggesting that the women with vulval lesions be examined by a person with interdisciplinary skills [3]. But it might not be possible for every primary or second line health facility to have trained staff with these facilities. In women with coloured skin chronic inflammation due to any reason leads to destruction of pigment cells resulting in depigmentation or hypopimentation which might be alarming to the patient as well as the gynaecologist not experienced in management of vulval lesions. Although the exact prevalence rates are not known, vulval intraepithelial lesions or early vulval carcinoma are not common clinical entities and not every gynaecologist will be comfortable in deciding whether biopsy needs to be taken or not. In this scenario, vulval biopsy and histopathtology examination of every lesion will be required unless a proper risk score to detect high-risk lesions is constructed. There have been no prospective studies in which clinical features of patients with vulval lesions have been studied individually or in combination for prediction of malignant or premaligmant lesion of vulva and a scoring system has been attempted.

Therefore, the aim of this study was to determine the clinical associations of malignant and premalignant lesions of vulva (moderate to severe dysplasia and early invasive lesion) and to formulate a scoring system to differentiate the high-risk lesion from a low-risk lesion on clinical grounds so as to decide for biopsy and referral.

Methodology

The study was conducted at tertiary care hospital in northern India. Seventy women referred to or presenting directly to the outpatient clinic in view of vulval complaints or randomly detected vulval lesion were enrolled in the study. The study was reviewed and approved by the Departmental Review Board, the Head of the Institution and CSIR. Seventy women with mean age of 46.7 years

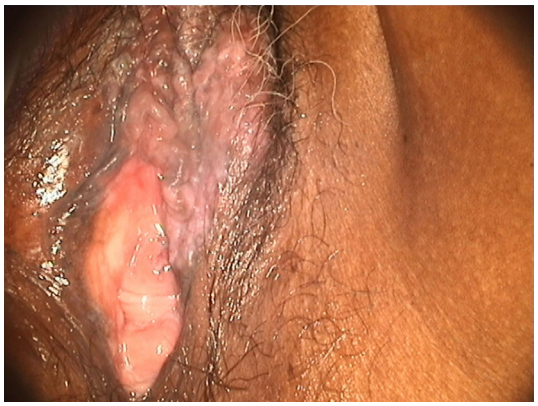

Fig. 1 Pictures of carcinoma in situ vulva without toluidine blue

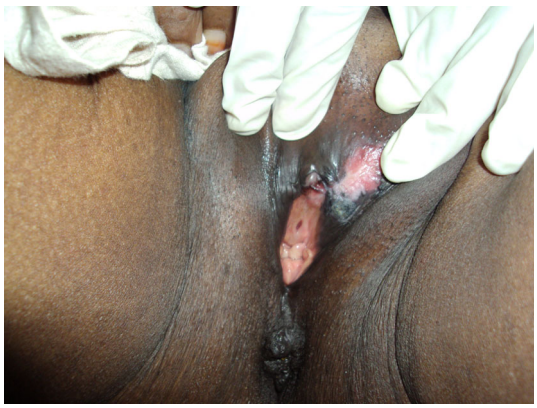

Fig. 3 Another picture of carcinoma in situ

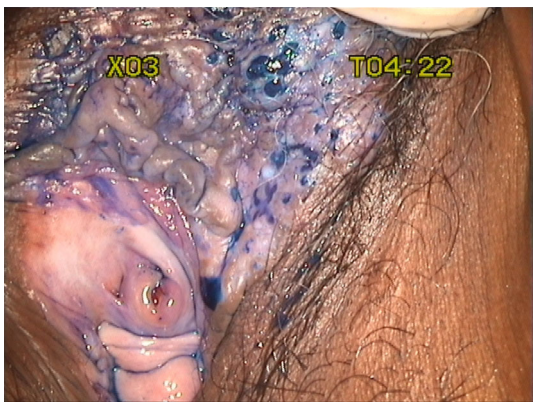

Fig. 2 Pictures of carcinoma in situ vulva after toluidine blue

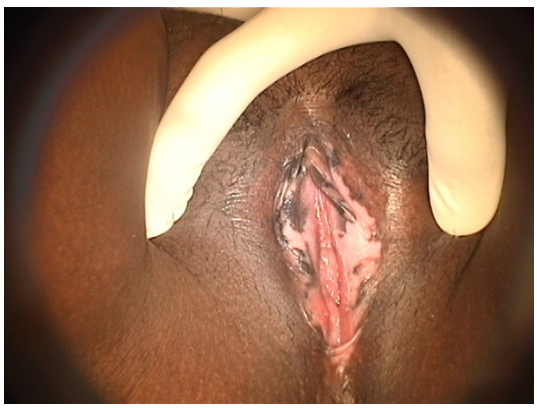

Fig. 4 Picture of benign lesion: early lichen sclerosus

Table 1 Complaint at the time of presentation

Presenting complaint	Total		Malignant/premalignant		Benign	
	$N = 66$	%	$N = 6$	%	$N = 60$	%
Itching	22	31.4	0	0	20	33
Itching and depigmentation	20	28.6	5	63.3	15	25
Asymptomatic	11	15.7	0	0	11	18.3
Depigmentation	10	14.3	0	0	8	13.3
Follow-up vulvectomy for VIN/Ca vulva	4	5.7	0	0	4	6.7
Vulval growth	2	2.9	1	16.7	1	1.7
Pain	1	1.4	0	0	1	1.7

Table 2 Duration of Symptoms

Duration	Total		Malignant/premalignant		Benign	
	$N = 66$	%	$N = 6$	%	$N = 60$	%
More than 12 months	25	37.1	4	66.7	21	33
6–12 months	10	15.7	2	23.4	19	30.6
3–5 months	11	15.7	0	0	10	14
Less than 3 months	20	31.4	0	0	20	32.4

Table 3 Age distribution

Age (years)	Total		Malignant/premalignant		Benign	
	$N = 66$	%	$N = 6$	%	$N = 60$	%
<20	1	1.5	0	0	1	1.7
21–35	16	24.2	1	24.2	15	25
36–50	23	34.8	2	34.8	21	35
51–60	19	28.8	2	28.8	17	28.3
>60	7	10.6	1	10.6	6	10

Table 4 Histopathology report of the patients

Histopathology	Frequency $N = 66$	%
Squamuos cell carcinoma with invasion <5 mm	3	4.8
Moderate to severe dysplasia	3	4.8
Mild dysplasia	5	8.1
Lichen sclerosus	10	12.9
Squamous hyperplasia	11	16.1
Plasma cell vulvitis	1	1.6
Chronic inflammation	30	46.8

(SD 13.2) and range of (18–75 years) were initially enrolled into the study after informed consent. Women with acutely tender vulval lesions with duration of less than 2 weeks were not included so that cases of acute infective lesions were excluded.

A thorough history was taken, followed by general physical and systemic examination. Vulva was thoroughly inspected for any lesions. After inspecting the vulva with naked eye under bright light, it was visualized using a colposcope. (Figs. 1, 3, 4) Acetic acid (5 %) was applied to vulva for a period of 3 min followed by naked eye and vulvoscopic examination for any acetowhite areas. Thereafter 1 % aqueous solution of Toluidine blue [4] was applied to the vulva including area from mons pubis to perianal area, bilateral labia majora, minora and introitus. The dye was allowed to stay over the area for 3 min, meanwhile colposcopic examination of cervix and vagina was performed. The dye was then sponged using 1 % acetic acid and areas of toluidine blue retention (Fig. 2) were observed. After washing off toluidine blue with acetic acid hyperkeratosis was viewed as areas retaining pale blue stain [5]. The vulva was viewed in detail by naked eye and under magnification for number and distribution of lesion, pigment change, ulcer, elevated area (surface topography), hyperkeratosis, extension over urethra, anal canal and vagina. The presence of induration on palpation along with naked eye examination was evaluated separately. At the end of the procedure 4-mm punch biopsy was performed under local anaesthesia. The biopsy specimen was formalin fixed and examined by an experienced pathologist. Clinical parameters: age, presenting complaints, duration of symptoms, asymmetrical distribution of the lesion, the presence of depigmentation, ulceration, hyperkeratosis, acetowhite changes after acetic acid application, surface elevation on naked eye or colposcopy, induration on palpation and toluidine blue stain retention were the characteristics that were studied for each woman.

Association of clinical features with histopathology report of preneoplastic lesion and early malignancy was analysed. Statistical analysis was performed using Statistical Package for Social Sciences (Version 15.0) with κ^2 test or Fisher exact test as appropriate. A score was formulated using the factors which were significantly

Table 5 Association of clinical features with histopathology report suggestive of malignant or premalignant lesion

Risk factor	Total no. of women positive for this factor	Malignant/premalignant histopathology report	Benign histopathology report	*P* value
Age >60	15	2	13	0.414
Postmenopausal status	39	4	35	0.525
Duration of symptoms more than 6 months	41	6	35	**0.049** (FE)
Asymmetrical distribution of lesion	12	6	6	**0.0000 (FE)**
Depigmentation	57	6	51	0.399 (FE)
Hyperkeratosis	28	5	23	**0.045(FE)**
Ulceration	20	3	17	0.254 (FE)
Acetowhite changes with acetic acid	32	4	30	0.432(FE)
Surface elevated on colposcopy	7	5	2	**0.0000 (FE)**
Induration on palpation	6	4	2	**0.0002 (FE)**
Toluidine test positive	41	6	35	**0.04(FE)**

FE Fisher exact test

Bold denote the statistically significant results

associated with malignant or premalignant lesion. The performance of the test was evaluated using area under the ROC curve.

Results

Initially 70 women were enrolled for the study. Itching alone or in association with depigmentation was the most frequent symptom amongst the enrolled women present in 60 % of women (Table 1). In almost 50 % of women (Table 2) the complaints were of more than 6 months duration. The age distribution in the study population is shown in Table 3. In two women biopsy was not performed as the lesion appeared to improve on application of antifungal medication. Two more women refused biopsy after enrolment. These four women were excluded from the study and final analysis was performed for 66 women in whom biopsy was performed. The histopathology reports of the patient are shown in Table 4. In 91 % of women (60/66) the lesion was benign. Almost 17 % of women had mild, moderate or severe dysplasia or early invasive lesion on histopathology examination. Cases with moderate to severe dysplasia were classified as high-grade lesions. The cases of mild dysplasia were classified as benign lesions and managed conservatively on follow-up. They were not included in the high-grade lesion group as there is not enough evidence that these lesions will progress to invasive lesion [6]. Age, duration of symptoms, presenting complaints, asymmetrical distribution of the lesion, the presence of depigmentation, ulceration, hyperkeratosis, acetowhite area, surface elevation on naked eye or colposcopy, induration on palpation and toluidine blue stain retention were the factors that were statistically analysed for association with malignant or premalignant lesion. Age more than 60 years, depigmentation, acetowhite change after application of acetic acid and ulceration were not significantly associated with high-grade lesion. The association of clinical features with premalignant or early neoplastic lesion is depicted in Table 5. A score of 6 was formulated by including the 6 clinical factors that were significantly associated with the high-grade lesions i.e. duration more than 6 months ($P = 0.049$), hyperkeratosis ($P = 0.045$), surface elevation ($P = 0.0000$), induration ($P = 0.0002$), positive toluidine blue staining ($P = 0.04$) and asymmetrical distribution of the lesion (0.000). A score of three or more was found to be significantly associated with high-grade lesion ($P = 0.0000$; Fisher exact test). The optimal cutoff point was found to be ≥ 3 with 100 % sensitivity and 91.7 % specificity and area under the curve 98.9 ± 1.1 % with $P < 0.001$. ROC is depicted in Fig. 5.

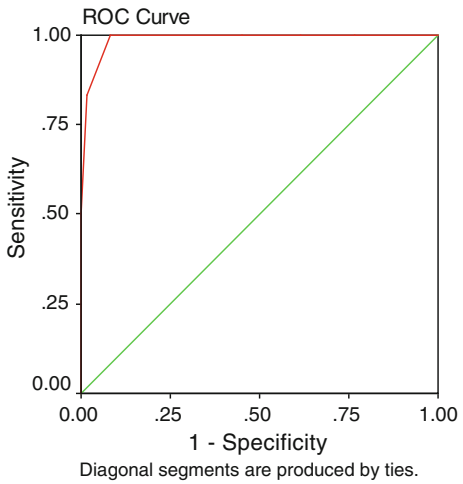

Fig. 5 ROC for scores one to six for detection of malignant or premalignant lesion

Table 6 Score distribution according to histopathology result (malignant/premalignant histopathology report) and sensitivity/specificity of each score for detecting high-grade lesion

Score	Malignant/premalignant histopathology report		Total	Sensitivity (%)	Specificity (%)
	No	Yes			
0	13	0	13	100	0
1	10	0	10	100	39
2	10	0	10	100	55
3	22	0	22	100	91.7
4	4	1	5	83	98.3
5	1	2	3	50	100
6	0	3	3	0	100

Discussion

We have designed a scoring system for women with vulval lesion which has sensitivity and specificity for detecting vulval preneoplastic and early neoplastic lesions. Previously some of these factors have been reported to be associated with high-grade lesions but have never been incorporated in the form of a score. Duration of symptoms more than 6 months rules out symptoms due to infective condition. Excessive surface keratinisation, hyperkeratosis is seen by naked eye as a white, plaque-like area that is often strikingly white even without acetic acid application. In women with lichen sclerosus, with malignant/premalignant transformation are more likely to be associated with hyperkeratosis than in women without malignancy [7]. In our study hyperkeratosis is significantly associated with malignant/premalignant lesions in women with vulval lesions. Toluidine blue test has been studied by Joura et al. [4] and has been reported to have high negative predictive value. But another study gives conflicting reports with false positive rate of 26.9 % and false negative rate of 85.8 % [2]. Induration is a relatively subjective feature and has never been studied. But any chronic infiltrative lesion is likely to distort the epithelial and subepithelial architecture resulting in induration. Any surface elevation in an ominous sign reflecting an underlying cellular proliferation and HPV warts are the main differential in women with surface elevation in the vulval lesion. The presence of acetowhite area after application of 5 % acetic acid was not significantly associated with premalignant lesion in our study as opposed to cases of cervical premalignant lesion. Also, acetowhite changes in the vestibular and vulval areas have been documented to be normal vulval finding previously [8].

All these features found to be associated with high-grade lesions individually have low predictive value for vulval neoplasia. Therefore, we studied the combination of these features for evaluation of high-risk lesions and this score was formulated. For each score there was a certain probability to find or exclude a high-grade lesion. This has been summarised as sensitivity and specificity for high-grade lesions at different thresholds depicted in Table 6. No high-grade lesion had a total score of less than four. If the score was less than three then even mild dysplasia was ruled out. Thus in the current study biopsy could have been avoided in 50 % (33/66) of women without missing out on high-grade lesions. We would suggest that in patients with unifocal lesion having a score of 5/6 or more a wide local excision could have been attempted in the first place as the procedure could have been diagnostic as well as therapeutic for moderate to severe dysplasia and adequate sample could have been obtained to rule out invasive disease. This score needs to be validated in different and larger population.

Conclusion

This clinical grading of the lesion will prove to be more useful for facilities where easy referral to experts in vulval disorders is not available and there is not much experience in handling vulval lesions. This simple and effective tool can identify lesions with high malignant potential with the least invasive technique to decide for biopsy and referral. Repeated biopsies can also be avoided in patients following up for chronic non-neoplastic disorders of vulva and those who have been managed surgically in the past for neoplastic or preneoplastic lesion.

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References

1. Maclean AB. Vulval cancer: prevention and screening. Best Pract Res Clin Obstet Gynaecol. 2006;20:379Y95.
2. Micheeletti L, Barbero, Trivelli MR, et al. Unreliability of toluidine blue test in the early diagnosis of vulvar neoplasia. Cervix LFGT. 1985;3:171–4.

3. Micheletti L, Bogliatto F, Lynch PJ. Vulvoscopy: review of a diagnostic approach requiring clarification. J Reprod Med. 2008;53(3):179–82 Review.
4. Joura EA, Zeisler H, Lösch A, et al. Differentiating vulvar intraepithelial neoplasia from nonneoplastic epithelial disorders: the toluidine blue test. J Reprod Med. 1998;43(8):671–4.
5. Singer A, Monaghan J, Quek SC, Deery ARS. Vulvar Intraepithelial Carcinoma. In: Singer A, Monaghan J, editors. Lower genital tract precancer-colposcopy, pathology and treatment. 2nd ed. Oxford: Blackwell Science; 2000. p. 233–289.
6. Scurry J, Edward J, Wilkinson EJ. Review of terminology of precursors of vulvar squamous cell carcinoma. J Lower Genital Tract Dis. 2006;10(3):161–9.
7. Jones RW, Sadler L, Grant S, et al. Clinically identifying women with vulvar lichen sclerosus at increased risk of squamous cell carcinoma. J Reprod Med. 2004;49:808Y11.
8. van Beurden M, van der Vange N, de Craen AJ, et al. Normal findings in vulvar examination and vulvoscopy. Br J Obstet Gynaecol. 1997;104(3):320–4.