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A clinicopathological spectrum of vulvar and vaginal lesions in a tertiary health care centre in North India: A five-year experience

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ABSTRACT

Introduction: Spectrum of lesions occur on the vulvar/vaginal regions ranging from non-neoplastic to precursor lesions to malignancy, however, these lesions presents with non-specific symptoms due to which they get unnoticed and progress. An early histopathologic examination is of paramount importance for a rapid diagnosis and initiation of treatment. Thus this study was done to study the clinicopathological spectrum of vulval and vaginal lesions with an emphasis on precursor and malignant lesions.
Materials and Methods: Present study was a five-year retrospective study including all the vulval and vaginal specimens that were sent for histopathological examination.
Results: A total of 66 cases were studied ranging from non-neoplastic to malignant lesions. Maximum cases were found in the fourth decade. The most common presenting complaints were found to be ulcers, pain and nodular growth. Amongst the non-neoplastic lesions, Bartholin cyst (12.1%) was the most common lesion. Vulval/vaginal intraepithelial Neoplasia II was found to have a slightly more occurrence than VIN I and III. Neoplastic lesions formed the bulk of cases with moderately differentiated squamous cell carcinoma (18.2%) being the most common diagnosis.
Conclusions: Early identification and histopathological diagnosis are essential for recognization and its further categorization to initiate an early and proper treatment.

1. Introduction

The vulva and vagina are usually affected by multiple diseases of various etiologies, but due to its particular anatomic and physiologic characteristics an additional diagnostic and therapeutic difficulty is created.[1] The vulva and vaginal lesions vary from precursors lesions to malignancy which can be attributed to its exposure to various sex hormones as well as physiological and pathological effects.[2] Inflammatory dermatosis like Lichen sclerosis (LS) which is also known as lichen sclerosis et atrophicus (LSA) commonly occurs on the vulval/vaginal regions causing substantial discomfort (intractable itching, soreness, constipation, and dyspareunia) and morbidity (narrowing and burying of the clitoris, and atrophy labia minora) and is found associated with vulvar intraepithelial neoplasia (VIN) of the differentiated type and invasive squamous cell carcinoma.[3] In addition to dermatological lesions, various cystic lesions like Bartholin cyst and Gartner cyst also occur in the vulva and vagina. In general cystic lesions of the vulva and vagina are typically benign and asymptomatic and do not require intervention. However, cysts arising in women older (>40 years) who are fixed or associated with pain or bleeding need an early diagnosis and treatment.[4] Vulvar/vaginal intraepithelial neoplasia (VIN) is an increasingly common problem, particularly among women in their 40s. It's a premalignant condition with no screening strategies for

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its prevention and progression, though detection can be done by visual assessment a histopathological confirmation is always needed.[5] Despite the increasing incidence of precursor lesions these are missed or misdiagnosed clinically leading to the development of a well developed squamous cell carcinoma. Such suspected lesions need an early histopathological diagnosis for confirmation for prevention and early treatment.[6]

2. Materials and Methods

This study was a five-year retrospective study (November 2017 to November 2021) carried out in Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India and included all samples from vulvar and vaginal lesions. A total of sixty-six samples including punch biopsy and excisional biopsies that were sent for histopathologic examination from various departments like surgery, gynaecology and dermatology were included. The patient's clinical data including age, presenting complaints along other relevant investigations were noted. Received biopsy samples (66) were processed routinely and Hematoxylin and Eosin staining was performed on formalin-fixed paraffin-embedded tissue.

3. Results

The study included a total of 66 patients with vulvar and vaginal lesions. The patient's age ranged from 16 to 94 years with a peak incidence in the 4th decade of life (16 cases, 24.2%) followed by the 3^{rd} decade (15 cases, 22.7%) (Table 1). The most common presenting complaints were found to be ulcer, pain or an ulceroproliferative growth (34.8%) followed by vulval/vaginal discomfort (28.7%). Other complaints noted were nodular and warty growth (16.6%), Itching (15.1%), cystic swelling/growth (12.1%), discharge (10.6%), papule/patch (7.5%) and pigmented lesion (1.5%) (Table 2).

A wide spectrum of lesions ranging from non-neoplastic to precursor lesions to malignancy was observed (Table 3). Amongst the three categories incidence of non-neoplastic lesions were observed to be maximum (48.5%) with a total of 32 cases followed by 30 cases of malignancy (45.5%). However, the precursor lesions were observed to be only 4, (6.0%) of the total cases Among the non-neoplastic lesions, cystic lesions formed the majority of cases with a maximum incidence of Bartholin cyst (8 cases) (12.1%). The next most common lesions to be reported were vulvitis and vaginitis with a total of 7 cases (10.6%), while fibroepithelial polyp also showed a similar incidence (10.6%). Dermatological inflammatory lesions like lichen sclerosis constituted a total of 4 cases (6.1%). Other lesions to be noted were Verrucous Hyperplasia, 3 cases (4.5%), Gartner cyst (3.1%) and vulvar tuberculosis (1.5%). In patients diagnosed as Lichen Sclerosus Atrophicus presenting complaints like itching, dysuria and vulvar/vaginal discomfort were observed. In cases diagnosed as Bartholin cyst, a cystic nodular swelling usually on the lateral/postero-lateral vaginal wall was observed with vaginal discomfort as the chief presenting complaint. A total of 4 precursor lesions were noted, with a slight increase in the incidence of Vulval/vaginal intraepithelial lesion II (VIN II) comprising of 2 cases (3.0%) followed by the equal incidence of Vulval/vaginal intraepithelial lesion I(VIN I) (1.5%) and Vulval/vaginal intraepithelial lesion III (VIN III) (1.5%). A hypertrophied and or thickened plaque were the associated presenting complaints with these lesions.

Amongst the neoplastic lesions, squamous cell carcinoma formed the bulk of cases (25 cases, 38%). The common associated presenting complaint was either an ulcer with pain or an ulceroproliferative growth over the vulva and vagina. Within this category, on histology, moderatory differentiated carcinomas were 12 cases (18.2%) while well-differentiated carcinomas were 10 cases (15.2%). 3 cases were categorised as poorly differentiated carcinoma (4.6%). Other neoplastic lesions reported were metastasis from other organs (2 cases, 3.0%), Poorly differentiated carcinomas (2 cases, 3.0%). A single case of adenoid cystic carcinoma (1.5%) was also noted.

Table 1: Age distribution of patients

Age (years)	Number of cases	Percentage
0-10	0	0
11-20	3	4.5
21-30	7	10.6
31-40	15	22.7
41-50	16	24.2
51-60	12	18.2
61-70	8	12.2
71-80	3	4.5
81-90	2	3.1
91-100	0	0
Total	66	100

Table 2: Distribution according to the presenting complain

Presenting Complain	Number of cases (n=66)	Percentage
Itching	10	15.1
Discharge	7	10.6
Nodular and warty growth	11	16.6
Papule/patch over vulva/vagina	5	7.5
Cystic swelling/growth	8	12.1
Ulcer, pain/ulceroproliferative growth	23	34.8
Pigmented lesion	1	1.5
Vulvar/vaginal discomfort	19	28.7

Table 3: Distribution of vulvar and vaginal lesions

Category	Diagnosis		Number of cases	Percentage
1. Non neoplastic	a. lichen sclerosis atrophicus		4	6.1
	b. Bartholin cyst		8	12.1
	c. Gartner cyst		2	3.1
	d. tuberculosis		1	1.5
	e.vaginal/vulval inflammation		7	10.6
	f. verrucous hyperplasia		3	4.5
	g.Fibroepithelial polyp		7	10.6
Total			32	48.5
2. Precursor Lesions	a. VIN1(vulval/vaginal intraepithelial neoplasia I)		1	1.5
	b. VIN II (vulval/vaginal intraepithelial neoplasia II)		2	3.0
	c. VIN III (vulval/vaginal intraepithelial neoplasia III)		1	1.5
Total			4	6.0
3. Malignant Lesions	a. squamous cell carcinoma	Well-differentiated carcinoma	10	15.2
		Moderatory differentiated carcinoma	12	18.2
		Poorly differentiated carcinoma	3	4.6
	b. adenoid cystic carcinoma		1	1.5
	c. metastasis from other organs		2	3.0
	d. poorly differentiated carcinoma		2	3.0
Total			30	45.5
			66	100

4. Discussion

A wide spectrum of lesions occurs on the vulvar and vaginal lesions with a varied range of presenting complaints. Amongst the commonest noted are vulval and vaginal discomfort, itching and pain. Some lesions may present as cystic or nodular swelling without pain and may get unnoticed.[7] Due to these overlapping clinical features as well as for early prevention of precursor lesions to malignancy, a biopsy for histopathological examination is of utmost importance for a confirmatory diagnosis.[8] In this study, the age range varied from 16 years to 94 years with a peak incidence in the 4^{th} decade. The next common age group was the 3^{rd} decade. It was observed that the incidence of non-neoplastic lesions was more common in females of the younger age group (below 30 years) while the precursor and malignant lesions were more common in females of middle and older age group (above 30 years). Maximum vulval and vaginal lesions observed were categorised under the non-neoplastic category accounting for 32 cases (48.5%). 8 cases (12.1%) of Bartholin cyst were observed. In a study of 40 cases of the vaginal cyst by Hoang LN et al[6] cases of Bartholin's duct cysts (27.5%) were noted. Histopathology of Bartholin cyst showed variable sized dilated ducts lined by transitional epithelium and surrounded by mucous glands in the cyst wall (Figure 1 a,b). The next most common lesion noted was vulvitis and vaginitis with a total of 7 cases (10.6%), while fibroepithelial polyp also showed a similar incidence (10.6%). Histopathology of fibroepithelial polyp showed loose myxoid stroma covered by squamous epithelium (Figure 2). Lichen sclerosis was noted in 4 cases (6.1%) with histological features of thinning of the epidermis, presence of a broad eosinophilic bundle of hyalinized collagen in the dermis, along with dilated and congested blood vessels.(Figure 3 a,b). A total of 3 cases (4.5%) of verrucous hyperplasia was noted whose histopathological features were finger-like projections with sheets of cells without invading the underlying stroma (Figure 4). 3 cases (4.5%) of Gartner cyst (3.1%) were noted showing dilated glands lined by cuboidal epithelium (Figure 5) and 1 case of vulvar tuberculosis (1.5%) was observed. Precursor lesions were noted in 4 cases (6.0%). Most of these cases were reported in middle age and elderly women. VIN has a spectrum of clinical and histopathological appearances and can be divided into two subtypes: usual type VIN, which is caused by a persistent infection with high-risk Human papillomavirus (HPV), and differentiated type VIN, which is associated with lichen sclerosis (LS). (10)However, the WHO classification with the three subtypes VIN 1, 2 and 3 is still widely under which it is graded as VIN 1 (mild dysplasia), VIN 2 (moderate dysplasia) and VIN 3 (severe dysplasia) which suggests a biologic continuum of VIN lesions. (11). Vulval/vaginal intraepithelial lesion II (VIN II) comprising of 2 cases (3.0%) and its histopathological features showed dyskeratocytes involving the upper two-thirds of the dermis (Figure 6 a) while in Vulval/vaginal intraepithelial lesion I(VIN I), the dyskerocytes were limited to upper one-third of

the epidermis (Figure 6 b) and Vulval/vaginal intraepithelial lesion III (VIN III) showed the involvement of entire epidermis with dyskeratosis and few mitotic figures with the intact basement membrane, each of them constituted one case (1.5%). Neoplastic lesions constituted the next largest category after non-neoplastic with a total of 30 cases (45.5%). Amongst the neoplastic lesions, squamous cell carcinoma formed the bulk of cases (25 cases, 38%). In a retrospective study of 41 patients with histologically proven vulvar cancer by Singh N et al, nearly 97.56% of the cases were squamous cell carcinomas.[9] On histopathology 10 (15.2%) cases showed mild pleomorphism well-formed keratin pearls and ample amount of keratinisation as was labelled as well-differentiated squamous cell carcinoma (Figure 7 a) Maximum cases (12.18.2%) showed moderate differentiation and keratinisation and were labelled as moderatory differentiated carcinomas (Figure 7 b)). 3 cases were categorised as poorly differentiated squamous cell carcinoma (4.6%). Other neoplastic lesions reported were metastasis from another organ (2 cases, 3.0%). Secondary vulval/vaginal malignancies are due to local extension from gynaecological malignancies such as cervical or vulvar cancer. Other sites of origin may include the colon, rectum, breasts and kidneys. The origin of the vulvar/vaginal metastasis can be established based on immunohistochemistry. The prognosis for vaginal metastasis is poor, as it is usually associated with disseminated disease.[10]

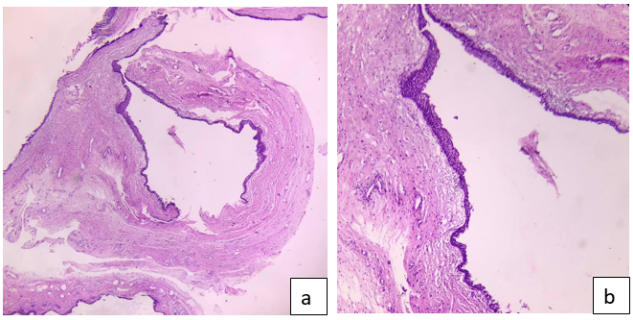

Fig. 1: a: Bartholin cyst (H and E X5); **b:** Bartholin cyst (H and E X10)

2 cases (3.0%) were of poorly differentiated carcinomas (Figure 8). A single case of adenoid cystic carcinoma (1.5%) was also noted. Adenoid cystic carcinoma in the vulva or vagina is extremely rare. It is an epithelial tumour that usually originates in the salivary glands, submandibular glands, and minor salivary glands. Though this tumour is malignant, has a low local recurrence, and rarely leads to distant metastasis. Because of rarity, the prognosis of Adenoid cystic carcinoma in the vagina is unknown.[11]

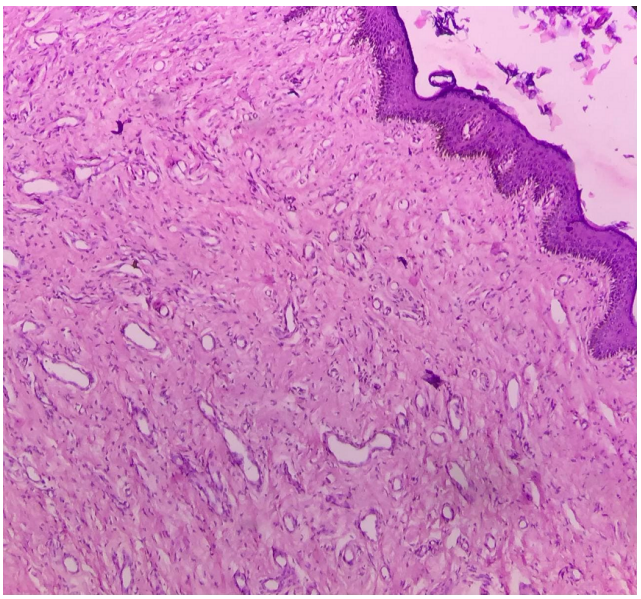

Fig. 2: Fibroepithelial polyp (H and E X10)

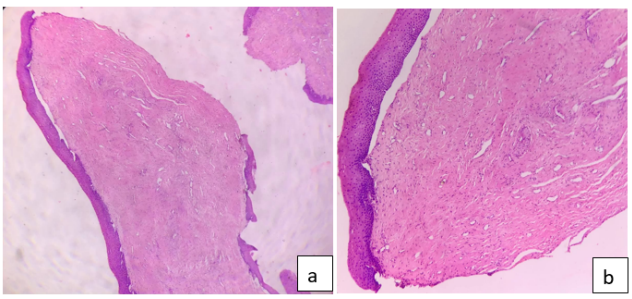

Fig. 3: a: Lichen sclerosis atrophicus (H and E X10); **b:** Lichen sclerosis atrophicus (H and E X40)

5. Conclusion

A considerable variety of lesions occur on the vulva and vagina which are encountered in our routine practice and often cause a diagnostic dilemma for the pathologist. In this five years prospective study we reported the overall incidence of various lesions over the vulva and vagina presenting to our tertiary hospital located in north India. As the incidence of these lesions especially the precursor and neoplastic lesions have been increasing, an early clinical diagnosis and biopsy are essential and at the same time, an early and proper histopathological diagnosis keeping in mind the other entities occurring on the same sites is necessary for initiation of timely treatment, management and follow up of the patient.

6. Source of Funding

None.

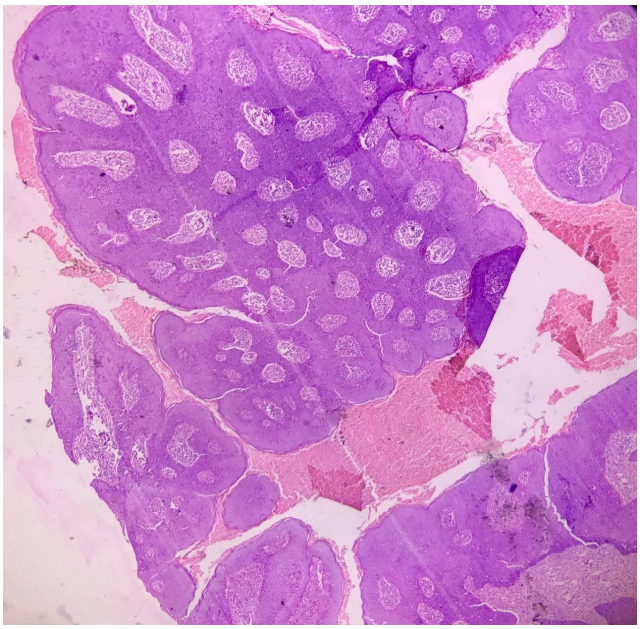

Fig. 4: Verrucous hyperplasia (H and E X10)

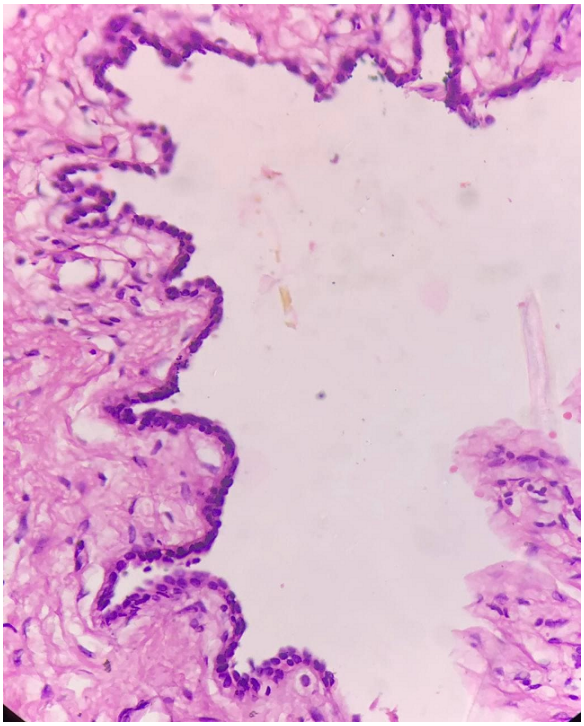

Fig. 5: Gartner cyst (H and E X10)

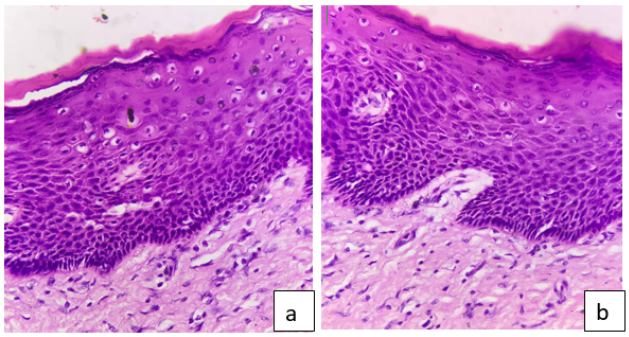

Fig. 6: a: Vaginal intraepithelial neoplasia Grade 2, VIN 2 (H and E X40); **b:** Vaginal intraepithelial neoplasia Grade 1, VIN 1 (H and E X40)

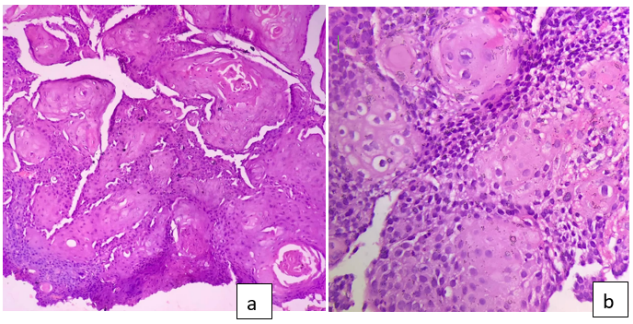

Fig. 7: a: Well differentiated squamous cell carcinoma (H and E X10); **b**: Moderately differentiated squamous cell carcinoma (H and E X40)

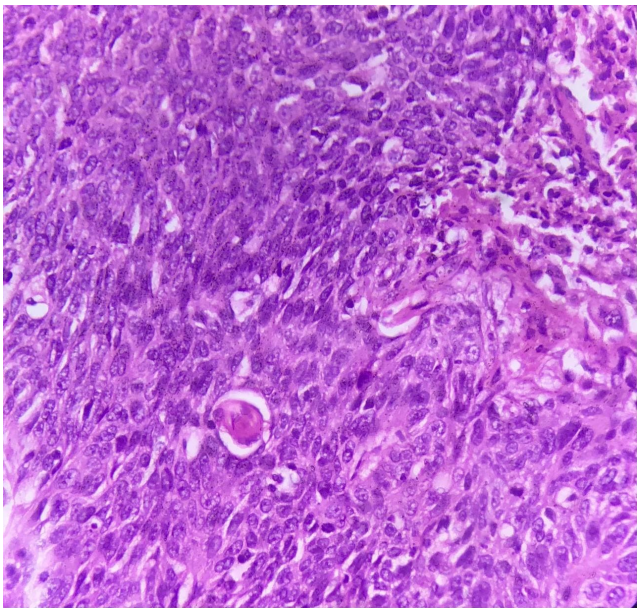

Fig. 8: Poorly differentiated maligancy (H and E X40)

7. Conflict of Interest

None.

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