

Pap smear findings in uterine prolapse: a coincidence or indicator for impending malignancy

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Received February 20, 2015. Accepted March 4, 2015

Abstract

Background: Uterine prolapse is a health problem affecting millions of women globally. If left untreated, it can lead to infection, bleeding, metaplasia, and, rarely, cancer.

Objective: To evaluate the Pap smear finding in patients with uterine prolapse and compare it with nonprolapse cases.

Materials and Methods: This was a retrospective study design. Pap smear data of 1,427 patients from January 2012 to December 2012 were analyzed for the history of prolapse and the pap smear findings such as squamous metaplasia, hyperkeratosis, parakeratosis, and reactive cellular changes.

Result: Of 1,427 patients, a total of 233 patients complained different degrees of uterine prolapse, and, in comparison to nonprolapse cases, the pap smear findings of squamous metaplasia, hyperkeratosis, and parakeratosis were statistically significant. Reactive cellular changes were more common in prolapse cases, but the data were not statistically significant.

Conclusion: Uterine prolapse is a health problem affecting millions of women globally. Today, by using an effective test such as pap smear, which is a simple, quick, and painless screening method for early diagnosis and subsequent reduction in the progression to invasive carcinoma, we are now positioned to more effectively evaluate this condition and to enhance our understanding of its outcomes through the pursuit of novel research.

KEY WORDS: Pap smear, uterine prolapse, cervical metaplasia

Introduction

A uterine prolapse is a weakening of the pelvic floor muscles. As the muscle mass becomes feeble, there is insufficient support for uterus, and thus it could go down in the direction of vagina. Uterine prolapse is a health problem affecting millions of women globally. The global occurrence of uterine prolapse is 2%–20%. It is noted that, in India, one in five of women paying a visit to private clinics in Bengal, Delhi, Punjab, and Uttar Pradesh are with uterine prolapse. The incidence of uterine prolapse is 7.6% in Northern India and 20% in Eastern India.^[1] There are three degrees of uterovaginal prolapse. The state

where the complete uterus shall protrude outside the vulva, bringing with it both the vaginal walls is called procidentia. If left untreated, it can lead to infection, bleeding, and, rarely, cancer.^[2] The carcinoma of the cervix and uterine prolapse are usual in developing nations, but the combination of these two is an unusual prevalence.^[3]

Cervical cancer is the leading cancer among women in terms of incidence rates in 2 of the 12 Population Based Cancer Registries (PBCRs) in India and has the second highest incidence rate after breast cancer in the rest of the PBCRs.^[4] Cervical cancer usually develops very slowly. It starts as a precancerous condition called dysplasia also termed as cervical intraepithelial neoplasia (CIN). CIN starts at the transformation zone, especially in relation to the squamous metaplasia and reserve cell hyperplasia. Any grade of dysplasia can progress to Ca in situ, even invasive carcinoma.^[5] Cervical cytology by Papanicolaou (Pap) is an effective method of screening for cervical premalignant and malignant conditions.^[6]

Chronic inflammation is known to be associated with malignancies of the skin, penis, lungs, and liver. Direct mechanical

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Website: <http://www.ijmsph.com>

DOI: 10.5455/ijmsph.2016.20022015375

Quick Response Code:



irritation, combined with longstanding chronic inflammation of third-degree prolapse, can make liable to the occurrence of cervical malignancy.^[7] In analyzing these various reasons why carcinoma of the cervix is seen so infrequently with procidentia, the cornified cervical epithelium becoming resistant to the development of carcinoma and less vaginal secretion, absence of infection, and free drainage appear to be the commonest reasons given for the protection against carcinoma. Carcinoma is more easily produced in animals by chemical irritation rather than traumatic irritation.^[8]

As the prolapse uterus is very common and irritating condition which may rarely lead to precancerous changes in the cervix or may be a protective phenomenon against the development of malignancy is a debatable issue. The purpose of this study is to show the significant association of squamous metaplasia (the precursor for cervical cancer), hyperkeratosis, and parakeratosis, and as the Pap smear finding in patients with uterine prolapse, which is sparsely represented in the literature despite the high incidence of the later.

Materials and Methods

We conducted a hand review at the Pathology Laboratory of New Civil Hospital to evaluate all Pap smears reported between January 1, 2012 and December 31, 2012. A total of 1,427 cervicovaginal cytology slides were wet-fixed immediately in absolute alcohol, stained with Pap stain, and reported according to the Bethesda system 2001.^[9]

History and symptoms were recorded. The cytological findings such as squamous metaplasia, hyperkeratosis, parakeratosis, and reactive cellular changes were noted specifically in patients with or without uterine prolapse. Data were analyzed statistically to see the significant relation of these findings with prolapse of uterus.

Result

A total of 1,427 patients' Pap smears were screened from the period of January 2012 to December 2012. Of these, 1194 patients were without any history or physical examination finding of prolapse, and 233 patients were having complained or presented physical examination findings of different degrees of uterine prolapse. We have separated patients according to different age groups, and various Pap smear findings were compared in both the groups such as with or without uterine descent.

In the group of patient with descent, maximum patients were in the age group of 51–60 years, and the second peak was in the age group of 31–40 years, while in the patients without descent, the highest number of cases was in the age group of 31–40 years.

Of 1,427 cases, we have received only 5 cases of ASCUS in 233 uterine prolapse cases. Any squamous or glandular malignant or premalignant cervical lesion was not found in our study.

Discussion

The literature is overwhelmed with evidences supporting the importance of early detection of precancerous lesions of the cervix by cytological examination using Pap smear. Few cases of cervical cancer have been reported in prolapsed uterus in the last few years, and most of them have been observed in underdeveloped countries.^[10] Some hypotheses attribute this lower risk to the displacement of the cervix to from its natural environment, which may decrease the neoplastic process of viral infection. Others argue that continual injury in cervical epithelium is the origin of these tumors.^[11]

In a study done by Guthrie and Bache, the thirty-two surgeons offer no explanation for the infrequent association of carcinoma of the cervix with complete procidentia. Sixteen suggest various reasons for the rarity; less vaginal secretion and free drainage was mentioned nine times; cornification of the cervical epithelium resists the development of carcinoma was suggested nine times; the lessened area of infection in a prolapsed cervix may safeguard the patient from developing carcinoma was spoken of four times. Sixteen men mentioned chronic irritation and chronic ulceration of the cervix in prolapse but do not believe it the cause of carcinomatous development.^[6]

In our study, maximum cases of prolapse uterus were in the age group of 51–60 years age group while in nonprolapse cases were in 31–40 years age group. Procidentia with carcinoma of the cervix may be influenced by the age group, for carcinoma of the cervix is usually seen in relatively younger women; the older women thus have gone safely through the period when carcinoma usually develops, finally developing prolapse without carcinoma; those of the younger age may develop carcinoma of the cervix and are cured or succumb before procidentia develops; moreover, carcinoma of the cervix by causing fixation of the uterus may prevent the development of procidentia. It is well-known that carcinoma is used to develop at points of fixation in other organs and systems.^[6] As shown in Table 1, in both the groups of patients with or without uterine descent, percentage of metaplasia increases

Table 1: Distribution of patients in different age groups with metaplasia as a pap smear finding

Age group (years)	With descent		Without descent	
	Total cases	Metaplasia, N (%)	Total cases	Metaplasia, N (%)
≤20	3	1 (33.3)	14	1 (7.14)
21–30	31	9 (29.03)	355	57 (16.05)
31–40	52	20 (38.46)	423	76 (17.96)
41–50	48	23 (47.91)	265	52 (19.62)
51–60	59	30 (50.84)	89	20 (22.47)
61–70	36	20 (55.55)	38	15 (39.47)
≥71	4	2 (50)	10	4 (40)
Total	233	105 (45.06)	1194	225 (18.84)

Table 2: Statistical significance of different pap smear findings in patients with and without descent

Pap smear finding	With descent, N (%)	Without descent, N (%)	P
Incidence of metaplasia	105 (45.06)	225 (18.84)	<0.0000001
Reactive cellular changes	87 (37.33)	382 (31.99)	0.13
Bacterial vaginosis	23 (9.87)	140 (17.72)	0.48
Hyperkeratosis	84 (36.04)	63 (5.27)	<0.0000001
Parakeratosis	33 (14.16)	61 (5.10)	0.00000073

as the age advances, and, as shown in Table 2, we have got squamous metaplasia in 45.06% of patients with descent when compared with only 18.84% of patients without descent. The squamous metaplasia is statistically highly significant Pap smear finding in patient with uterine prolapse as shown by *P* value in Table 2.

Hyperkeratosis indicates large number of anucleated squamous cells present in Pap smear. Hyperkeratosis is often diagnostic of benign leukoplakia or a reaction to a chronic irritation as seen in uterine prolapsed inflammation or chemical or physical trauma to the cervical mucosa. On rare occasions, hyperkeratosis may overlie a significant lesion or dysplastic condition. Hyperkeratosis in the form of ≥ 2 clusters of anucleated squamous cells could be an indicator of underlying low-grade squamous intraepithelial lesion.^[12] Parakeratosis is a protective surface reaction of the squamous epithelium. It is characterized by the formation of multiple layers of compact miniature squamous cells with pyknotic nuclei. Parakeratosis may overlie and mask a significant epithelia abnormality such as dysplasia.^[13] Hyperkeratosis may persist separately or in association with parakeratosis, and this should be reported with caution in cases of uterine descent. In our study, incidence of hyperkeratosis and parakeratosis were 36.04% and 14.16% of cases, respectively, in patients with descent, while it was only 5.27% and 5.10%, respectively, in patients without descent. Both these Pap smear findings were also statistically significant.

Reactive cellular changes were also percentagewise more number in patients with descent [37.33%] when compared with without descent group (31.99%), but the data are not statistically significant as shown by χ^2 -test *P* value. Keratinization and pigmentation of vaginal mucosa and ulceration of the prolapsed tissue are caused by friction, congestion, and circulatory changes in the dependent part of the prolapse-decubitus ulcer. It needs to be differentiated from cancer of the cervix. Rarely, carcinoma develops over the decubitus ulcer.^[14] The ulcers seen on the irritated cervixes with prolapse are more often of the decubitus type. When the prolapse is complete, there is torsion of the blood vessels which greatly reduces circulation with resultant venous stasis. The process is very much like that seen in varicose ulcers of the leg; there is

edema, venous congestion, and sclerosis of the skin, which lead to atonic ulceration, with little tendency to cicatrization. The ulcers which often appear are trophic in type. When the situation of carcinoma is considered, it is always in an area of good blood supply and in an area of chronic irritation.^[8] Chronic genital prolapse may be associated with carcinoma of the cervix and more rarely with carcinoma of the vagina.^[10]

So, from this study we have found that squamous metaplasia, hyperkeratosis, and parakeratosis were statistically significant findings in patients with uterine prolapse when compared with patients without prolapse. Whether these findings can be correlated as definite increase risk for cervical cancer is a debatable issue. We have tried to correlate the findings with definite association, but its practical implication in predicting as a significant risk factor or a protective factor for development of cervical malignancy, "the infrequency of carcinoma of the cervix with complete procidentia," requires more research in terms of more number of patients in study, and very important is their follow-up study such as how many patients of prolapse develop malignancy when compared with patients without descent.

We personally think that this area is still not taken into consideration despite the large burden of prolapse disease in underdeveloped countries. So, our motive is to sensitize the people regarding these findings and to open a gate of further research in this undiscovered area, which may be helpful in further understanding of cervical malignancy.

Conclusion

Uterine prolapse is an age-old condition, a condition from which many women have faced and many clinicians have attempted to correlate its positive or negative association with cervical malignancy. The slow historical progress of the field and the challenges that we face today in terms of considering uterine prolapse as a blessing or a curse for development of cervical malignancy reflect the very intricacies of this disorder that fascinate and inspire us to do further research in this direction.

Cervical cytology by Pap smear is a simple, safe, quick, and effective test to identify CIN and carcinoma of cervix at an early stage; it can be done at the first visit to the health clinic, thereby helping the clinicians in early and more efficient management of the patients. It also suggests a need for further evaluation or follow-up. Today, by using an effective test such as Pap smear for early detection of malignancy, we are now positioned to more effectively evaluate this condition and to enhance our understanding of its outcomes through the pursuit of novel research.

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How to cite this article: Taylor HJ, Bhagat VM, Patel PR, Patel A, Italiya SL. Pap smear findings in uterine prolapse: a coincidence or indicator for impending malignancy. *Int J Med Sci Public Health* 2016;5:819-822

Source of Support: Nil, **Conflict of Interest:** None declared.