

Audit on preinvasive and invasive neoplasm of the cervix and associated pathologies among the women with uterine prolapse in rural women of North India

Seema Dayal, Arun Nagrath¹

Department of Pathology and ¹Obstetrics and Gynecology, Rural Institute of Medical Sciences and Research, Etawah, Uttar Pradesh, India

ABSTRACT

Background: Uterine prolapse is a common complaint in gynecology. It is defined as an abnormal downward displacement or protrusion of the pelvic structures in the vaginal canal. **Aim:** The aim of this study was to know the gross and microscopic cervical changes in uterine prolapse and their association with clinical findings. **Materials and Methods:** The present study was conducted in the histopathology section of the Department of Pathology in Rural Institute of Medical Science and Research, Saifai, Etawah, Uttar Pradesh, on hysterectomy specimens with prolapse uterus from January 2012 to May 2015. **Results:** The minimum age of patients with prolapse was 25 years and maximum age was 70 years, maximum number of patients belonged to 41–50 years age group (38.72%). Common clinical complaint was something coming out per vagina (53.61%). On gross examination, hypertrophy of cervix was a common pathology (46.38%). Histopathology examination of prolapse uterus showed chronic cervicitis (87.65%), cervical intraepithelial neoplasia I (21.70%), and others, but carcinoma cervix was not present. **Conclusion:** Prolapse uterus was a common gynecological complaint among rural women, usually clinically presenting with something coming out per vagina. Grossly, the cervix appeared hypertrophied in the majority. Histopathological examination showed chronic cervicitis in bulk. Chronic cervicitis paves the way for premalignant and malignant lesions of cervix, though cervical carcinoma is rare in prolapse uterus. Prolapse uterus must be diagnosed early so as to provide early treatment before the complications arise.

Key words: Cervix, rural women, uterine prolapse

INTRODUCTION

Utero-vaginal prolapse is a common clinical complaint in gynecological practice. It occurs in about 316 million women worldwide, which comprises 9.3% of all women. Stallworthy in 1971 reported that genital prolapse accounts for 20% of all gynecology surgeries.^[1] The word prolapse is derived from the Latin word procedure, which means

to fall. It is defined as the downward displacement or protrusion of pelvic structures in the vaginal canal due to the weakening or damage to pelvic supports. Normally, when a woman strains, there is no descent of the uterus, while in the advanced cases of the prolapse, the cervix of the uterus may be pushed down to the level of the vulva and even seen outside the vulva. In extreme cases, the whole uterus and most of the vaginal wall may be extruded from the vagina. Women suffering from utero-vaginal prolapse may experience significant disruption of their recreational, professional, social, and sexual activities. The

Address for correspondence: Dr. Seema Dayal, Department of Pathology, Rural Institute of Medical Sciences and Research, Saifai, Etawah, Uttar Pradesh, India. E-mail: seemadayal5@gmail.com

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most important etiological factor in prolapse is atonicity and asthenia of the ligamentary supports that follow menopause. This has been attributed to estrogen deficiency. Prolapse uterus is more common following child birth, although it may remain asymptomatic. Approximately, 50% of parous women have some degree of urogenital prolapse.^[2] Pelvic organ prolapse is graded via Shaw system, Baden–Walker system, and the pelvic organ prolapse quantification system.

According to Shaw system, vaginal descent is classified into the following types – 1st degree, i.e., descent of the cervix into the vagina, 2nd degree – descent of the cervix up to introitus, 3rd degree – descent of the cervix outside the introitus, and finally 4th degree or procidentia – descent of the entire uterine body uterus outside the introitus.

Baden’s system of grading is similar to Shaw’s, but uses hymen as reference point.

Clinically, patients with prolapse may be asymptomatic or symptomatic. Women usually complaint of something coming out per vagina. Grossly, *in utero* vaginal prolapse, cervix is usually hypertrophied, thickened, keratinized, everted, ectropion, and it is not uncommon to find trophic ulcers, hyperpigmentation, and nabothian follicles on the cervix. On histopathology examination, chronic cervicitis, keratinization, squamous metaplasia, carcinoma, and intraepithelial neoplasm are common findings with utero-vaginal prolapse. A study with clinical details and cervical changes in prolapse uterus has not been done from this region. Hence, this study was planned with the objective to know the gross and microscopic cervical changes in uterine prolapse and their association with clinical findings.

MATERIALS AND METHODS

This study was conducted in the histopathology section of the Pathology department from January 2012 to May 2015. Detailed clinical history and relevant clinical findings were also taken in a predesigned pro forma, which also included number of children, history of abortion, contraceptive use, and socioeconomic status. Detailed cervical examination was done to rule out other differential conditions such as vulval cyst or tumor, congenital elongation of cervix, fibroid polyp, cyst of anterior vaginal wall, and chronic inversion. All specimens were fixed in 10% formal saline and these formalin-fixed specimens were thoroughly examined grossly. On gross examination, length of cervix, hypertrophy of cervix, surface keratinization, everted or inverted cervix, erosion, polyp, and nabothian follicles were included. Sections from prolapse uterus cervix were taken at 3–4 μ m. Hematoxylin and eosin stain was applied, if required, and additional sections were also taken.

Statistical analysis was done by percentage.

Ethical clearance was taken from Institutional Ethical Committee.

RESULTS

The minimum age of patients presenting with prolapse uterus was 25 years and maximum age of patients presenting with prolapse was 70 years. The maximum numbers of patients belonged to the age group of 41–50 years (38.72%) [Table 1]. Among the associated clinical details, multi parity was found more (85.53%) followed by under nutrition (66.38%) [Table 2]. The majority of patients of uterine prolapse were symptomatic. Most of the women complained of something coming out per vagina (53.16%) followed by backache (22.12%), micturition disturbances (26.80%), coital difficulties (4.25%), vaginal discharge (3.40%), and least common were bowel dysfunction and postcoital bleed, both aggregating (1.70%) [Table 3]. The gross examination of cervix showed the following pathologies: Hypertrophy of cervix (46.38%), surface keratinization (32.34%), everted cervix (28.93%), nabothian follicle (27.23%), inverted cervix (25.10%), and erosion (3.82%); polyp and ulcer were least common accounting 0.85% and 0.42% each, respectively [Table 4].

On histopathology examination, chronic cervicitis (87.65%), surface keratinization (36.17%), nabothian follicle (13.11%), squamous metaplasia (11.05%), koilocytosis (4.68%), endocervical polyp (0.85%); and cervical intraepithelial neoplasia 1 (CIN 1) and CIN 2 were 21.70% and 1.27% diagnosed, respectively [Table 5].

DISCUSSION

Prolapse uterus is a common clinical complaint frequently encountered in gynecological practice. It is generally recognized that pelvic floor relaxation is a progressive

Table 1: Age of patients presented with prolapse uterus

Age of patients	Under 30 years	31-40 years	41-50 years	51-60 years	61-70 years	Total
Number of patients	6	75	91	52	11	235
Percentage of patients	2.5	31.91	38.72	22.12	4.68	

Table 2: Associated clinical details of patients presented with prolapse uterus

Clinical details	n (%)
Multiparity	201 (85.53)
Under nutrition	156 (66.38)
Constipation	80 (34.04)
Smoking	64 (27.43)
Surgery	47 (20.00)
Others	20 (8.51)

Table 3: Clinical findings of patients presented with prolapse uterus

Clinical findings	Under 30 years' age group (%)	31-40 years (%)	41-50 years (%)	51-60 years (%)	61-70 years (%)	Total (%)
Uterus descend in vagina protruding either at vulva or externally	1 (0.79)	31 (24.60)	52 (41.26)	38 (30.15)	4 (3.17)	126 (53.61)
Backache	1 (1.92)	11 (21.11)	24 (46.15)	14 (26.92)	2 (3.84)	52 (22.12)
Micturition disturbances	2 (5.71)	8 (22.85)	10 (28.57)	14 (40)	1 (2.85)	35 (14.89)
Coital difficulties	0	2 (20)	6 (60)	2 (20)	0	10 (4.25)
Vaginal discharge	0	4 (50)	2 (25)	2 (25)	0	8 (3.40)
Others	0	1 (25)	2 (50)	1 (25)	0	4 (1.70)

Table 4: Gross findings of cervix in patients presented with prolapse

Gross findings in cervix	Under 30 years (%)	31-40 years (%)	41-50 years (%)	51-60 years (%)	61-70 years (%)	Total (%)
Hypertrophy of cervix	2 (1.83)	35 (32.11)	42 (38.53)	26 (23.85)	4 (3.66)	109 (46.38)
Surface keratinization	3 (3.94)	22 (28.94)	31 (40.78)	16 (21.05)	4 (5.26)	76 (32.34)
Everted cervix	0	21 (30.88)	30 (44.11)	15 (22.05)	2 (2.94)	68 (28.93)
Nabothian follicle	2 (3.125)	20 (31.25)	28 (43.75)	10 (15.62)	4 (6.25)	64 (27.23)
Inverted cervix	1 (1.69)	12 (20.33)	34 (57.62)	11 (18.64)	1 (1.69)	59 (25.10)
Erosion	0	1 (11.11)	4 (44.44)	3 (33.33)	1 (11.11)	9 (3.82)
Polyp	0	0	1 (50)	1 (50)	0	2 (0.85)
Ulcer	0	0	0	0	1 (100)	1 (0.42)

Table 5: Histopathological findings of cervix in patients presented with prolapse

Histopathology findings	Under 30 years (%)	31-40 years (%)	41-50 years (%)	51-60 years (%)	61-70 years (%)	Total (%)
Chronic cervicitis	4 (1.94)	64 (31.06)	85 (41.26)	45 (21.84)	8 (3.88)	206 (87.65)
Surface keratinization	2 (2.35)	26 (30.58)	31 (36.47)	22 (25.88)	4 (4.70)	85 (36.17)
Nabothian follicle	2 (6.45)	11 (35.48)	11 (35.48)	3 (9.67)	4 (12.90)	31 (13.19)
Squamous metaplasia	2 (7.69)	9 (34.61)	11 (42.30)	3 (11.53)	1 (3.84)	26 (11.06)
Koilocytosis	1 (9.09)	2 (18.18)	4 (36.36)	4 (36.36)	0	11 (4.68)
Endo cervical polyp	0	0	1 (50)	1 (50)	0	2 (0.85)
CIN I	1 (1.92)	16 (30.76)	20 (38.46)	13 (25)	2 (3.84)	52 (22.17)
CIN II	0	2 (66.66)	0	1 (33.33)	0	3 (1.27)

CIN: Cervical intraepithelial neoplasia

process and menopause accelerates it. In prolapse, straining causes protrusion of cervix either to the level of vulva or extruded from the vagina.^[3] Prolapse uterus occurs mostly in postmenopausal and multiparous women. Major degree of prolapse can be considerably reduced by postnatal pelvic floor exercises, especially in the younger women and tone can also be regained by exercise. However, this does not apply to the menopausal women because their uterine supports have become atonic due to estrogen deficiency. Birth injury seen in parous women causes excessive stretching of pelvic floor muscles and ligaments that occur during child birth because of over stretched muscles and ligaments. The incidence of prolapse increases with age and approximately, 60% of elderly women have some degree of prolapse.^[4] Our result also confirms this because minimum number of cases were seen under the 30 years of age group (2.5%) and maximum cases were seen in the age group of 41–50 years (38.72%) [Table 1]. We did not find any case of prolapse above 70 years of age, although it is common in this age group. Reason behind this is that older women in rural population are neglected, they might not come to hospital for the treatment, so not registered.

Genital prolapse occurs due to the weakness of supporting structures. Incidence of prolapse is more in multiparous, which suggest that pregnancy and childbirth have an important impact on supporting function of pelvic floor. The present study also justifies this because multiparity (85.53%) was found in majority [Table 2]. Damage to the muscular, fascial support of pelvic floor, and changes in innervations contribute to the development of prolapse. Under nutrition was also seen (66.38%) among these women. Under nutrition was another factor for prolapse. Women in rural areas are uneducated, so least bothered about nutrition and healthy diet.

The prime clinical finding observed by women with prolapse was something coming out per vagina (53.16%) [Table 3]. The etiological factor in prolapse is atonicity and asthenia that follow menopause.^[5] Urogenital prolapse is more common following child birth and it may be asymptomatic. In India, especially among rural population, higher and severe degree of urogenital prolapse occurs in women who are delivered at home by dais because the patients are made to bear down before full dilation of the cervix, when the

bladder is not empty and second stage of labor is prolonged with undue stretching of the pelvic floor muscles, as episiotomy is not employed by the dais and circumstances force the poor women to resume their heavy work soon after delivery without any rest or pelvic floor exercise.

Second common symptom was mild sacral discomfort, i.e., backache (22.12%), which usually relieved by rest, reason for that may be body weakness caused due to lack of nutrition rich diet [Table 2].

Among micturition disturbances, imperfect control of micturition, stress incontinence, and frequency of micturition were common accounting for (14.89%). The imperfect control of micturition is caused by a lack of support to sphincter mechanism of the urethra. Frequency of micturition was also common, which is caused by chronic cystitis and by incomplete emptying of bladder due to downward displacement.

Coital disturbances were also seen (4.25%). It was also common among multiparous women with 3rd degree prolapse and procidentia. Cause for that is the degree of prolapse, which prevents penetration and orgasm due to lax outlet. Hence, this deteriorates the sexual activities of the women.

Some degree of vaginal discharge was also seen (3.40%). It occurs due to inflamed lacerated cervix and relaxation of vaginal orifice which allows organisms to invade vagina and produce vaginitis. One case of decubitus ulcer was also seen and friction of the decubitus ulcer may be the reason for discharge. Other less common clinical symptoms in prolapse were bowel dysfunctions and postcoital bleeding, both aggregating (1.70%).

Findings on gross examination of cervix in prolapse were also significant [Table 4]. Hypertrophy of cervix was the major gross finding seen in association with prolapse (46.38%). Supravaginal portion of cervix is well supported by Mackenrodt's ligament whereas vaginal portion of cervix gets prolapsed along with vagina, so the supravaginal portion gets stretched and elongated. The cervix may also show hypertrophy, edema, and congestion. Surface keratinization was the next common pathology seen with prolapse (32.34%). It occurs due to long-standing exposure to air and trauma due to tissue dryness. The surface epithelium of ectocervix in case of uterine prolapse may develop surface keratinization and hyperkeratosis which is called epidermalization. In the cervix of prolapse uteri, the clinical appearance is usually referred as leukoplakic. Microscopically, the process involves mainly the exocervix and is characterized by the appearance of granular and horny layer in the epithelium. This process is

not related to carcinoma and is best designated as keratosis. Surface keratinization was the next common pathology at microscopic level forming (36.17%).

Everted cervix

It is usually seen with cervicitis. It occurs as a result of cervical tears sustained during child birth. In cervicitis, on gross examination, cervix is everted and endocervical mucosa is hyperemic, edematous with surface granular changes. It was accounting for 28.93%.

Nabothian follicle/cyst

It is also called a retention cyst. They are grossly visible from surface as pearly gray vesicles. Bacterial infections and trauma cause squamous metaplasia, which blocks the opening of nabothian glands, mucous accumulates, and causes nabothian cyst.^[6,7] It was aggregating by 27.23%. Microscopically, they are lined by somewhat flattened single layer of mucin-producing endocervical epithelium.^[8] These similar microscopic findings were seen in the present study.

Erosion

Cervix erosion is a condition in which the squamous covering of the vaginal portion of the cervix is replaced by columnar epithelium. It is usually associated with chronic cervicitis. During chronic cervicitis, stroma of the cervix is edematous and the resistance of the squamous cells around the external os is reduced so that after a time, they desquamate and leave a raw red area denuded of epithelium around the external os, which represents the 1st stage in the development of erosion. Erosion formed in 3.82% in the present study.

Polyp

Polyps are common growths of the uteri cervix. They are localized, benign proliferation of endocervical mucosa, which may protrude through the external os.^[9,10] Cervical polyps are focal, hyperplastic protrusions of the endocervical folds. It is found during the fourth to sixth decade of life and in multigravida. In 40–50 years and 50–60 years age group, one patient with cervical polyp and endocervix polyp was seen both aggregating (0.85%). Endocervical polyp – they are relatively innocuous, inflammatory tumor that occurs in 2–5% of adult women. They are not true neoplasm, but probably the result of chronic inflammatory changes, i.e., “chronic polypoid cervicitis” Microscopically, they showed dilated endocervical glands, which are seen in an edematous inflamed and fibrotic stroma.^[11]

Decubitus ulcer

Ulcer is most commonly seen in posterior lip of cervix. It is common in third or fourth decade of prolapse, reason for that is congestion. It is the dependent part of prolapse because of impaired venous drainage due to compression of

uterine veins which results in ischemia causing necrosis and ulcer.^[4] At present, there is also one decubitus ulcer seen on the dependent part in the age group of 61–70 years (0.42%).

Chronic cervicitis

It is an extremely common condition in adult females at least at the microscopic level.^[8] Some degree of cervix inflammation is present in virtually all multiparous women and in some nulliparous women. It is seen in 80% of women with any gynecological complaints and is brought about by infection during abortion or child birth.

Cervicitis may be specific or nonspecific. Specific cervicitis is caused by tuberculosis, syphilis, granuloma inguinale, chlamydia, and chancroid. Nonspecific cervicitis is frequent. We also favor this because all the cervixes in present study showed nonspecific changes [Table 5 and Figure 1].

At the microscopic level, it is characterized by inflammation which usually have mononuclear cells mainly lymphocytes, macrophages and plasma cells with necrosis and granulation tissue [Figure 2].^[11] In the present study, chronic nonspecific cervicitis was the most common microscopic pathology (87.65%), which was quite similar (88.28%) in a study done by Dulhan *et al.*^[12]

Squamous metaplasia

It is used to designate the focal or extensive replacement of mucus-secreting glandular epithelium by stratified squamous epithelium. It is a complication of chronic cervicitis, though bacterial infections and trauma cause squamous metaplasia. After puberty, columnar epithelium undergoes squamous metaplasia near external os. As a result, the junction between squamous and columnar cells now shifts toward internal os. The area between previous squamous columnar junction and new squamous

columnar junction is termed as transformation zone. It is one of the most common sites of carcinoma formation. It was forming 11.26% of cervix pathology, although the maximum numbers of cases were among 41–50 years age group (42.30%). Squamous metaplasia is a reversible change and is not thought to be premalignant.

Koilocytosis

Human papilloma virus is currently considered to be an agent in cervix carcinogenesis.^[10] Human papilloma virus causes chronic cervicitis and it can also cause carcinoma cervix. The characteristic of Human Papilloma Virus is Koilocytosis which is superficial or intermediate mature squamous cells characterized by sharply outlined perinuclear vacuolation dense and irregular staining peripheral cytoplasm and enlarged nucleus [Figure 1].^[9] In present study Koilocytosis was 4.68%.

Carcinoma of the cervix is the most frequent of all the genital tract cancers.^[7,11] Carcinoma cervix is one of the most common malignancies worldwide, while the incidence of malignancy is on the decline, it is still very high in the developing countries. Its incidence varies from 21.3% to as high as 50% in different Indian cities. It occurs in the transformation zone as carcinoma intraepithelial neoplasm and then progress through carcinoma *in situ* to invasive carcinoma. Invasive squamous cell carcinoma develops from a histologically well-defined precursor lesion.^[13] Cervical dysplasia is a cytological term used to describe cells which resembles the cell of carcinoma cervix. CIN refers to the histopathological description where part or whole of the thickness of cervix epithelium is replaced by cells showing varying degree of dysplasia.

CIN I, when the atypical changes involve lower one-third of the epithelium, it is termed CIN I.^[10] The atypical changes are

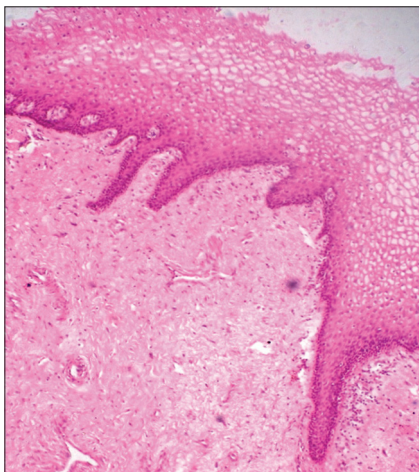


Figure 1: Section of cervix showing acanthosis, koilocytosis in epidermis, and it is moving deep in dermis whereas subepidermal region shows chronic inflammatory cells infiltrate (H and E, $\times 10$)

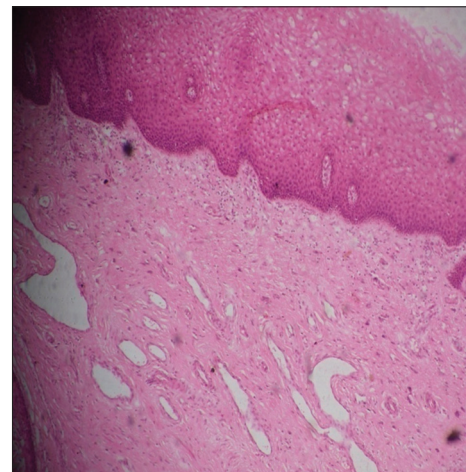


Figure 2: Section of cervix showing squamous cells, which shows acanthosis in epidermis, and in subepidermal, there are chronic inflammatory cells that infiltrate predominantly lymphocytes (H and E, $\times 10$)

increased nuclear size, hyperchromasia, increased mitotic rate, increased nuclear: Cytoplasmic ratio, and loss of cellular polarity.^[7] The atypical changes become more severe with increased grades of CIN and carcinomatous changes.

When atypical changes involve one-third–two-third of the epithelium but not complete thickness is called CIN II.

While in CIN III, it involves more than two-third thickness of epithelium.

The present study also constituted CIN I (21.70%) and CIN II (1.27%). However, no case of CIN III was seen in women with prolapse cervix. Pant^[14] diagnosed 52.91% cases of CIN I, 32.78% cases of CIN II, and 9.65% cases of CIN III in his study.

Dulhan *et al.*^[12] diagnosed 1.36% and Pant^[14] diagnosed 1.5% cervical cancer in their studies. But in our study, there was not a single case of carcinoma cervix in prolapse uterus. Swamy and Chattopadhyay^[4] and Kumar and Malhotra^[15] also stated that for unknown reason, carcinoma cervix is rare in prolapse uterus. But, some gynecologists believe that because of pooling of blood in prolapse uterus, malignancy is rare.

CONCLUSION

Prolapse uterus is a common condition in women of rural population usually encountered in gynecological practice. Clinically, the patient complains of something coming out per vagina. Grossly, hypertrophied, surface keratinization, and everted cervix are common findings. Histopathology of these prolapse uterus showed chronic cervicitis as a common pathology, although CIN I and CIN II were also seen. Chronic cervicitis is the primary step for premalignant and malignant cervical lesions. However for unknown reasons, cervical malignancy is rare in prolapse uterus. Hence, common efforts must be taken for early diagnosis of cervical pathologies in uterine prolapse before the complications arise.

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Conflicts of interest

There are no conflicts of interest.

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