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Research Article

A clinico-morphological study of glandular hyperplasias of uterine cervix

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ABSTRACT

Background: Non neoplastic lesions of uterine cervix form a major bulk of the Diagnosis in histopathological departments. Some of the non-neoplastic lesions of uterine cervix mainly exuberant processes like glandular hyperplasias are prone to varying extents of misinterpretation. This can lead to potentially adverse consequences for the patient in the form of inappropriate treatment. But, studies on non-neoplastic lesions are comparatively less.
This is an attempt to study the clinico morphologic features of glandular hyperplasias of uterine cervix.
Methods: The present study is a retrospective study conducted using histopathology records of 2years (June 2013 to May 2015) in the department of Pathology, at a tertiary care hospital in south India. The study included 811 specimens of uterine cervix obtained either in the form of biopsies or hysterectomy specimens
Results: 44 cases of Glandular hyperplasias of uterine cervix were encountered in the present study. In the present study uterine cervix is the most frequently occurring lesion, seen in 20 (2.47%) cases, followed by Microglandular hyperplasia in 13 (1.6%), Diffuse laminar endocervical glandular hyperplasia in 7 (0.86%), and Florid deep glands in 4 (0.49%).
Conclusions: Glandular hyperplasias of uterine cervix arise in the reproductive age. Early age of occurrence in the present study compared to other studies can be attributed to early marriages and childbearing in Indian women.
As diagnosis rests on histologic characteristics in routinely stained sections, familiarity with these lesions by pathologists is essential to avoid over diagnosis and treatment.

Keywords: Glandular hyperplasias, Uterine cervix, Over diagnosis, Treatment

INTRODUCTION

Gynaecological specimens form the substantial proportion of the workload in most of the histopathological departments. Non neoplastic lesions of the cervix form a major bulk of the Diagnosis. Some of the non-neoplastic lesions of uterine cervix mainly exuberant processes like glandular hyperplasias are prone to varying extents of misinterpretation.[1] This can lead to potentially adverse consequences for the patient in the form of inappropriate treatment.[2]

Non-neoplastic lesions of uterine cervix are common, but there are very few publications on the subject compared to neoplastic diseases. Familiarity with these lesions by pathologists is needed to avoid over diagnosis and treatment.[3]

This is an attempt to know more about the clinico morphologic aspects of glandular hyperplasias of uterine cervix.

METHODS

The present study is a retrospective study conducted using histopathology records of 2 years (June 2013 to May 2015) in the department of Pathology, Dhanalakshmi Srinivasan Medical College & Hospital, Siruvachur, Perambalur, Tamilnadu.

The study included 811 specimens of uterine cervix obtained either in the form of biopsies or hysterectomy specimens. All inadequate biopsy specimens were excluded from the study. A detailed clinical examination including age, parity, clinical findings and provisional diagnosis were collected from the Medical records department.

All the specimens received at histopathology section were fixed in 10% formalin. The macroscopic findings of the hysterectomy specimens were examined and recorded, followed by fixation in 10% formalin for 24 hours. The hysterectomy specimen was later sampled carefully and tissue pieces were processed. The entire tissue piece of the biopsy specimen was submitted for processing. After routine processing, sections were cut at 4-6 µ thickness and stained routinely using Hematoxylin and Eosin stain.[4] These stained sections were analyzed by light microscopy.

RESULTS

44 cases of Glandular hyperplasias of uterine cervix were encountered in the present study.

Age wise distribution of Glandular hyperplasias of uterine cervix encountered in the present study show highest number of cases of 18 in the age group of 40-49 years, followed by, 17 in 30-39, 5 in 20-29, and 4 in 50-59 (Table 1).

Table 1: Age wise distribution of Glandular hyperplasias of uterine cervix.

Age range (yrs)	No. of cases
20-29	5
30-39	17
40-49	18
50-59	4
Total	44

Excessive vaginal bleeding and pain abdomen are the most common presenting complaints seen in 11 cases each, followed by mass per vagina and white discharge per vagina in 10 each, Irregular vaginal bleeding in 4, retention of urine and Pain during menstruation in 2, and mass per abdomen, burning micturition, Constipation and fever in 1 case each (Table 2).

Different lesions encountered in the study are shown in the table below (Table 3).

Table 2: Presenting complaints of the cases studied.

Presentation	No. of cases
Excessive vaginal bleeding	11
Mass per vagina	10
Pain abdomen	11
White discharge per vagina	10
Irregular vaginal bleeding	4
Mass per abdomen	1
Retention of urine	2
Pain during menstruation	2
Constipation	1
Fever	1
Burning micturition	1

Table 3: Different of types of glandular hyperplasias of uterine cervix encountered in the present study.

Sr. No	Lesions	No. of cases	Frequency (%)
1	Diffuse laminar endocervical glandular hyperplasia	7	0.86
2	Florid deep glands	4	0.49
3	Microglandular	13	1.60
4	Tunnel clusters	20	2.47
	Total	44	5.43

In the present study tunnel clusters is the most frequently occurring lesion, seen in 20 (2.47%) cases, followed by Microglandular hyperplasia in 13 (1.6%), Diffuse laminar endocervical glandular hyperplasia in 7 (0.86%) , and Florid deep glands in 4 (0.49%).

Diffuse laminar endocervical glandular hyperplasia

Seven cases of diffuse laminar endocervical glandular hyperplasia are encountered in the study with a frequency of 0.86%.

Out of 7 cases, 3 each are seen in the age range of 20-29 and 40-49 years, and one in 50-59 with a mean age of 37 (Table 4).

Excessive vaginal bleeding, pain abdomen and white discharge per vagina are noted in three of the patients, irregular vaginal bleeding, mass per vagina and fever in one each (Table 5).

Leiomyoma is the associated pathology in two of the cases, chronic endometritis, salpingo-oophoritis, uterovaginal prolapse and dysfunctional uterine bleeding in one each.

Table 4: Age wise distribution of diffuse laminar endocervical glandular hyperplasia.

Age range (yrs)	No. of cases
20-29	3
30-39	0
40-49	3
50-59	1
Total	7

Table 5: Complaints in cases with diffuse laminar endocervical glandular hyperplasia.

Presentation	No. of cases
Excessive vaginal bleeding	3
Pain abdomen	3
White discharge per vagina	3
Irregular vaginal bleeding	1
Mass per vagina	1
Fever	1

Microscopy shows diffuse proliferation of well-differentiated endocervical glands limited to inner third of cervical wall. Glands are lined by bland, mucin containing columnar epithelium.

Florid deep glands

Four cases of florid deep glands are noted out of 811 cases studied with a frequency of 0.49%.

Table 6: Summary of cases showing florid deep glands.

Case	Age (yrs)	Presentation	Associated pathology
1	40	Pain during menstruation	Leiomyoma and Adenomyosis
2	35	Mass per vagina	Uterovaginal prolapse
3	35	Pain abdomen and white discharge per vagina	Chronic pelvic inflammatory disease
4	35	Mass per vagina and white discharge	Uterovaginal prolapse

Four cases of florid deep glands are observed. Three of the patients are 35 year old and the other is 40, with a mean age of 36 (Table 6).

Mass per vagina and white discharge per vagina is the presenting complaints seen in 2 cases, pain during menstruation and pain abdomen in one each.

Uterovaginal prolapse is the associated pathology in two of the cases, leiomyoma, chronic pelvic inflammatory disease and adenomyosis in one each.

Microscopy shows florid proliferation of endocervical glands deeply infiltrating the underlying stroma. The glands extend into the endocervical stroma to a depth of more than 9mm. Glands are lined by a single layer of columnar mucinous epithelium.

Microglandular hyperplasia

Microglandular hyperplasia is observed in 13 cases out of 811 cases studied with a frequency of 1.6%.

Out of 13 cases of microglandular hyperplasia 6 each are seen in the age group of 30-39 and 40-49 years, and 1 in 50-59 years (Table 7).

Table 7: Age wise distribution of cases of microglandular hyperplasia.

Age range (yrs)	No. of cases
30-39	6
40-49	6
50-59	1
Total	13

Excessive vaginal bleeding is the most common complaint seen in cases with microglandular hyperplasia in 6, followed by pain abdomen in 4, mass per vagina and white discharge per vagina in 3 each, irregular vaginal bleeding and burning micturition in one each (Table 8).

Table 8: Presenting complaints in cases with microglandular hyperplasia.

Presentation	No. of cases
Excessive vaginal bleeding	6
Mass per vagina	3
Pain abdomen	4
White discharge per vagina	3
Irregular vaginal bleeding	1
Burning micturition	1

Superficial tightly packed small glands lined by low columnar to cuboidal cells are noted in all the 13 cases and subnuclear vacuolation in 6 (Table 9).

Table 9: Microscopic features of microglandular hyperplasia.

Microscopic features	No. of cases
Superficial tightly packed small glands	13
Lining-low columnar to cuboidal	13
Subnuclear vacuolation	6

Tunnel clusters

Twenty cases of tunnel clusters are noted out of 811 cases

of uterine cervix studied with a frequency of 2.47%.

Table 10: Age wise distribution of tunnel clusters

Age range (yrs)	No. of cases
20-29	2
30-39	8
40-49	8
50-59	2
Total	20

Tunnel clusters are noted in the age group of 20-59 years. 30-39 and 40-49 years of age group show 8 cases each. 20-29 and 50-59 show 2 cases each (Table 10).

Most common presenting complaint in cases with tunnel clusters is excessive vaginal bleeding seen in 9 cases, followed by pain abdomen in 8, mass per vagina in 5, white discharge per vagina in 3, retention of urine in 3, pain during menstruation in 2, irregular vaginal bleeding in 2, mass per abdomen and constipation in one each (Table 11).

Table 11: Presenting complaints in cases with tunnel clusters.

Presentation	No. of cases
Excessive vaginal bleeding	9
Pain abdomen	8
Mass per vagina	5
White discharge per vagina	3
Retention of urine	3
Pain during menstruation	2
Irregular vaginal bleeding	2
Mass per abdomen	1
Constipation	1

In 9 out of 20cases of tunnel clusters parity is P3, P4 in 7, and P5 in 2, and P6 in 1 with a mean parity of 3.65 (Table 12).

Table 12: Obstetric history of the cases showing tunnel clusters.

Parity	No. of cases
P2	1
P3	9
P4	7
P5	2
P6	1

Microscopy shows lobular proliferation of glands appearing as closely packed tunnels with a small amount of intervening stroma. Tunnels are lined by cuboidal to columnar mucinous cells.

DISCUSSION

With the introduction of cervical screening programmes, and treatment of early premalignant squamous lesions of the cervix, pathologists are encountering more glandular lesions of the cervix[5]. A variety of pseudoneoplastic lesions may occur in the cervix and create problems in differential diagnosis. Failure to differentiate them from well-differentiated adenocarcinoma[1] can result in potentially major adverse consequences for the patient in the form of anxiety and inappropriate therapy[2]. The reverse mistake, the misdiagnosis of adenocarcinoma as a pseudoneoplastic lesion, may have equally adverse consequences for the patient[6].

Some of these lesions are rarely encountered and the pathologists are frequently unfamiliar with their appearance. Familiarity with these lesions by pathologists is necessary to avoid over diagnosis and treatment[3].

Awareness of their existence and knowledge of the features should enable the correct diagnosis to be made. This is an attempt to know more about these benign glandular lesions of the uterine cervix.

After excluding 9 inadequate biopsies, 811 cases were included in the present study.

Diffuse laminar endocervical glandular hyperplasia

Age range for diffuse laminar endocervical glandular hyperplasia in the present study was 25-50 years with a mean age of 37 and it was 22-48 and 37 in a study by M A Jones and R H Young3 (Table 13).

Table 13: comparison of age range and mean age for diffuse laminar endocervical glandular hyperplasia.

Study (no. of cases)	Age range (yrs)	Mean age (yrs)
Present study (n=7)	25-50	37
M A Jones and R H Young (1991) (n=7)	22-48	37

In the present study, associated pathology was leiomyoma in two of the cases, chronic endometritis, salpingo-oophoritis, uterovaginal prolapse and dysfunctional uterine bleeding in one each. In a study by M A Jones and R H Young[3] dysfunctional uterine bleeding was the associated pathology in 5 cases and leiomyoma in 2.

Microscopic features noted in the present study were diffuse proliferation of well-differentiated endocervical glands limited to inner third of cervical wall, sharply

demarcated from the underlying cervical stroma. Glands were lined by bland, mucin containing columnar epithelium. M A Jones and R H Young[3] noted similar findings in their study.

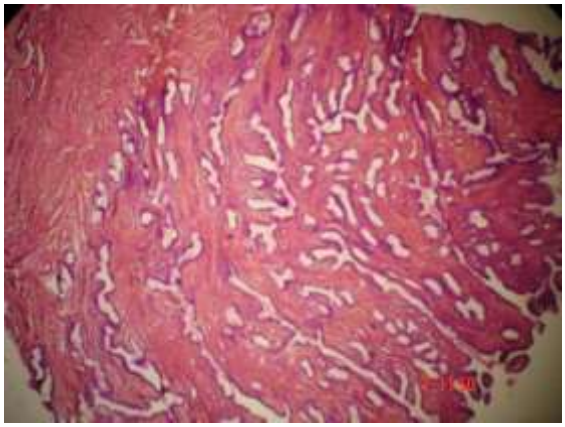

Figure 1: Diffuse proliferation of glands limited to inner third of cervical wall.

Florid deep glands

Four cases of florid deep glands of the uterine cervix were noted in the present study in the age of 35 (3cases) and 40 (1 case) years. In a study by D Daya and R H Young[4] two cases were noted in the age of 43 and 62 years.

In the present study mass per vagina and white discharge per vagina were the presenting complaints seen in 2 cases, and pain during menstruation and pain abdomen in one each.

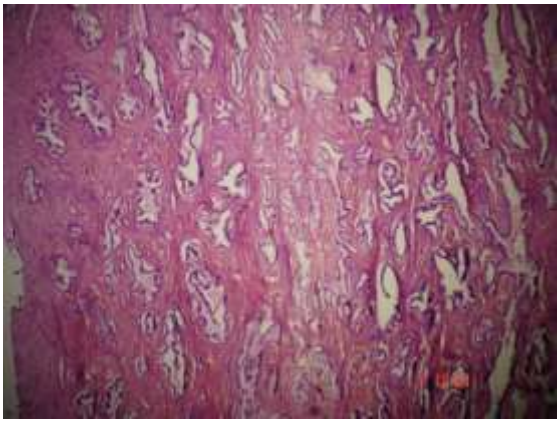

Figure 2: Florid proliferation of glands extending to a depth of more than 9 mm.

Perimenopausal bleeding was the presenting complaint noted in a study by D Daya and R H Young.[4]

In the present study, microscopy showed florid proliferation of endocervical glands deeply infiltrating the underlying stroma. The glands extended into the endocervical stroma to a depth of more than 9mm and were lined by a single layer of columnar mucinous epithelium. D Daya and R H Young[4] noted similar findings in their study.

Microglandular hyperplasia

Age range for microglandular hyperplasia was 32-52 years in the present study, 21-74 in a John C C et al study and 18-75 in R H Young and R E Scully study.[7,8]

Mean age for microglandular hyperplasia was 42 years in the present study, 35 in a John C C et al study and 40 in R H Young and R E Scully study (Table14).[7,8]

Table 14: Comparison of age range and mean age for microglandular hyperplasia.

Study (no. of cases)	Age range (yrs)	Mean age (yrs)
Present study (n=13)	32-52	41
John C C et al (1985) (n=43)	21-74	35
R H Young and R E Scully (1989) (n=5)	18-75	40

In the present study excessive vaginal bleeding was the most common presentation seen in cases with microglandular hyperplasia with 6 cases, followed by pain abdomen in 4, mass per vagina in 3, white discharge per vagina in 2, irregular vaginal bleeding and burning micturition in one each.

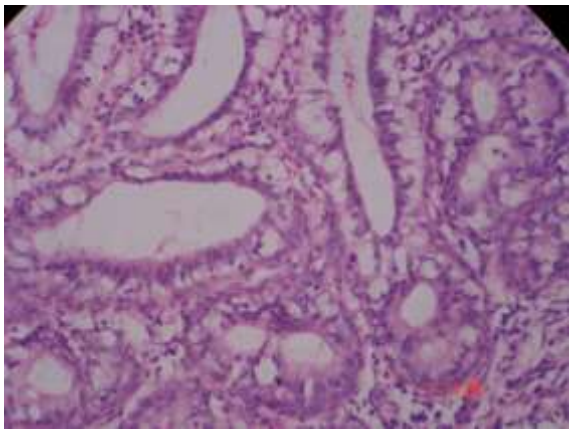

Figure 3: Tightly packed glands with subnuclear vacuolation.

In a John C C et al[7] study irregular menses was the commonest presentation seen in 37 cases, followed by spotting and pain during menstruation in three each.

In a study by R H Young and R E Scully[8], three of the patients were noted to have cervical polyp, early menopause in one and postmenopausal bleeding in the other (Table 15).

Microscopic features were similar in the present, John C C et al and R H Young and R E Scully's study and showed superficial tightly packed glands, lined by low columnar to cuboidal epithelium and subnuclear vacuolation were often present. R H Young and R E Scully noted few atypical findings in their study like-

solid sheet like proliferation of cells, pseudo infiltrative pattern, abundant stromal hyalinization, signet ring cells, hobnail cells and presence of moderate degree of nuclear atypicality.

Table 15: Comparison of mode of presentation in cases with microglandular hyperplasia.

Study (no. of cases)	Presentation	No. of cases
Present study (n=13)	Excessive vaginal bleeding	6
	Pain abdomen	4
	Mass per vagina	3
	White discharge per vagina	3
	Irregular vaginal bleeding	1
	Burning micturition	1
John C C et al (1985) (n=43)	Irregular menses	37
	Spotting	3
	Pain during menstruation	3
R H Young and R E Scully (1989) (n=5)	Cervical polyp	3
	Early menopause	1
	Post menopausal bleeding	1

Tunnel clusters

Age range for tunnel clusters was 20-55 years in the present study, 33-72 in a G H Segal and W R Hart[9] study and was 32-54 in an M A Jones and R H Young[10] study.

Mean age for tunnel clusters was 39 years in the present study and it was 55 in a G H Segal and W R Hart study and 45 in an M A Jones and R H Young study (Table16).

Table 16: comparison of age range and mean age for tunnel clusters.

Study (no. of cases)	Age range (yrs)	Mean age (yrs)
Present study (n=20)	20-55	39
G H Segal and W R Hart (1990) (n=29)	33-72	55
M A Jones and R H Young (1996) (n=14)	32-54	45

In the present study parity of the patients with tunnel clusters ranged from 2-6 with a mean parity of 3.6, and it was 0-5 and 2.1 in an M A Jones and R H Young study (Table17).

In a study by G H Segal and W R Hart 96.6% of the patients with tunnel clusters had a history of 2-11 prior pregnancies and 79.4% had at least 3 previous pregnancies. In the present study 95% of the patients had at least 3 previous pregnancies.

Table 17: Comparison of obstetric history of patients with tunnel clusters.

Study (no. of cases)	Parity range	Mean parity
Present study (n=20)	2-6	3.6
M A Jones and R H Young (1996) (n=14)	0-5	2.1

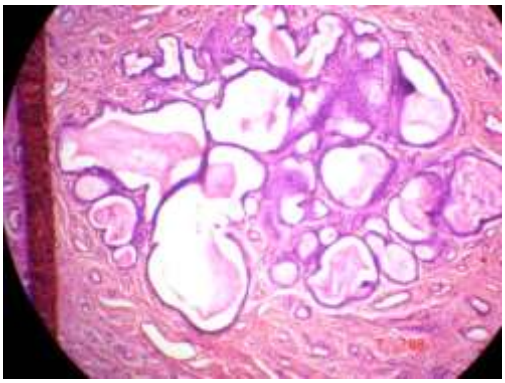

Figure 4: Lobular proliferation of glands appearing as tunnels.

Frequency of occurrence of tunnel clusters was 2.4% in the present study and 5.9 in a study by G H Segal and W R Hart (Table 18).

Table 18: Comparison of frequency of occurrence of tunnel clusters.

Study (no. of cases)	Frequency (%)
Present study (n=20)	2.4
G H Segal and W R Hart (1990) (n=29)	5.9

Microscopic features noted in the present study were presence of lobular proliferation of glands appearing as closely packed tunnels with a small amount of intervening stroma. Tunnels were lined by cuboidal to columnar mucinous cells. M A Jones and R H Young and G H Segal and W R Hart noted similar features, but M A Jones and R H Young have described proliferation of predominantly small-caliber, nondilated, closely packed glands and G H Segal and W R Hart proliferation of predominantly dilated tubular endocervical glands.[9,10]

CONCLUSION

Glandular hyperplasias of the cervix are mostly due to hormonal stimulation either during pregnancy or due to consumed pills. So most of them arise in the reproductive age and may remain and detected in the Perimenopausal or postmenopausal stage of life.

Early age of occurrence in the present study compared to other studies can be attributed to early marriages and childbearing in Indian women.

As diagnosis rests on histologic characteristics in routinely stained sections, familiarity with these lesions by pathologists is essential to avoid over diagnosis and treatment and vice versa.

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