Research Article

Patterns of epithelial cell abnormalities in Pap smears and its clinicopathological and demographic association: a descriptive study from Visakhapatnam city, Andhra Pradesh, India

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ABSTRACT

Background: Cervical cancer is one of the leading cancers amongst women. Periodic pap screening is the simplest way to diagnose precancerous lesions. Factors such as ignorance, poverty poorly developed public healthcare delivery system put women in urban slums at a disadvantage for receiving any health screening activity. Objectives of the present study were to know the prevalence of epithelial cell abnormalities of the cervix among the subjects and to study the association with clinical and demographic characteristics.

Methods: A camp based descriptive study was conducted in an urban ward. All women above the age of 20 years were included in the study. Data was recorded using a pretested questionnaire. Study variables included socio-demographic characteristics, symptoms of reproductive tract infection, findings of clinical examination, and Pap smear collection and evaluation. The latter was done from 194 women aged between 20-69 years. Pap smears were made by conventional Pap smear technique and reported according to The Revised Bethesda System of classification 2001(TBS).

Results: Among the 194 women, in 8 subjects, the smears collected were unsatisfactory for evaluation. Analysis was done in the remaining 186 subjects. Among the latter, in 83.9%, the smears were negative for intraepithelial lesions (NIEL) and 16.1% revealed epithelial cell abnormalities (ECA). Among those with ECA, Atypical cells of undetermined significance (ASCUS) was identified in 66.67%, Low grade squamous intraepithelial lesions(LSIL) in 16.67%, Atypical squamous cells-cannot exclude HSIL (ASC-H) and Atypical glandular cells-not otherwise specified (AGC-NOS) in 6.67% each and High grade squamous intraepithelial lesions (HSIL) in 3.33%. Epithelial cell abnormalities were more common in women in the age group of 30-60 years (80%), they were more common in those with age at marriage between 13-18 years (63.3%) and in those with age at first child birth between 15-19 years (56.7%).

Conclusions: Therefore there is a need for Pap screening at regular intervals through camp based approach in these populations to motivate the women, increase their awareness, ensure follow up and referral and timely intervention in appropriate cases.

Keywords: Cervical cancer, Periodic Pap screening, Epithelial cell abnormalities

INTRODUCTION

Cervical cancer is the second most common cancer among females worldwide and the most common cancer among females in developing countries including India.[1,2]

The importance of cervical cancer further lies in the fact, that the natural history has a long latent phase which enables detection and treatment of the premalignant lesions. The Pap screening test provides a simple, easy and effective means of identifying these lesions[2,3] and the

benefits exceed the costs involved.[4] The widespread use of Pap smear screening led to a dramatic reduction in the incidence and mortality of carcinoma cervix worldwide.[5] However similar results were not obtained in developing countries due to lack of its effective implementation.[6] In India, estimated new cases of cervical cancer were 90,708 in 2007.[7] The risk factor for cervical cancer is HPV.

Visakhapatnam is the second largest city in Andhra Pradesh with many slums. The slum dwellers are faced with problems of illiteracy, ignorance and poorly developed public health care delivery system. This study was conducted in one such urban slum, where women have inadequate health screening facilities, to know the prevalence of various epithelial cell abnormalities of the cervix and to correlate the Pap smear findings with clinical presentation and demographic characteristics of the subjects.

METHODS

It is a cross sectional descriptive study conducted over a period of 6 months from July 2011 to December 2011, among women attending the specialist screening camp organized in an urban slum in Malkapuram, Visakhapatnam. All women aged 20years and above were included in the study and those women who are known cases of cancer cervix were excluded. The data was recorded in semi structured pretested open ended questionnaire and all the subjects were clinically examined. Study variables included socio-demographic characteristics (age, education status, marital status, age at marriage, age at first child birth, parity), clinical symptoms and signs of reproductive tract infection and cytological nature of the cervical lesions as evaluated on Pap smears. Pap smears were made by conventional Pap smear technique, after visual inspection of the cervix following application of acetic acid (VIA test). Pap smears were collected using a Pap kit (endocervical brush, Ayre's spatula, and cotton swab) to ensure specimen adequacy. Smears were fixed immediately in 95% isopropyl alcohol and stained with Papanicolaou stain. Biopsies or periodic Pap screening was advised wherever necessary. Reporting of Pap smears was done according to The Revised Bethesda System of classification 2001 (TBS). According to this system, first the specimen adequacy was evaluated, (whether it is satisfactory or unsatisfactory) and the lesions were further categorized into NIEL (Negative for intraepithelial lesion) and epithelial cell abnormality (ECA). NIEL includes specific infections (organisms), non specific infections and other non-neoplastic conditions. ECAs are classified into Atypical squamous cells of undetermined significance (ASCUS), Atypical squamous cells-cannot exclude HSIL (ASC-H), Low grade squamous intraepithelial lesion (LSIL), High grade squamous intraepithelial lesion (HSIL), Atypical glandular cells-not otherwise specified (AGC-NOS), Adenocarcinoma *in situ* (AIS), Squamous cell carcinoma (SCC), Adenocarcinoma and Other malignancies. All the

Pap smears were interpreted by three pathologists independently to minimize error. The study was approved by the Ethics Committee of Andhra Medical College, Visakhapatnam.

RESULTS

A total of 209 women attended the screening camp. Out of them, 12 refused to have a Pap screening test and 3 were in their menstruation. The Pap test was done in the remaining 194 women; of these 8 smears were found unsatisfactory for evaluation. Therefore further analyses were performed in rest of the 186 subjects.

Majority (97.9%) of them were between 20-59 years. 90.3% were married and living with their husbands. The parity of the subjects ranged from 1-4 with 70.4% in the 1-2 parity range. None of the women had any history of multiple sexual partners. 24.7% of the women were illiterate and 44.1% had intermediate grade education. 87.1% were housewives (unemployed). There was no history of smoking or usage of oral contraceptive pills among the subjects.

Pap smears revealed epithelial cell abnormalities (ECA) in 30subjects (16.1%) and smears were negative for intraepithelial lesion (NIEL) in the remaining 156 subjects (83.9%).

Amongst the subjects with ECA, Atypical squamous cells of undetermined significance (ASCUS) were identified in 20 (66.67%), Low grade squamous intraepithelial lesion (LSIL) in 5 (16.67%), Atypical squamous cells-cannot exclude HSIL (ASC-H) in 2 (6.67%), Atypical glandular cells-not otherwise specified (AGC-NOS) in 2 (6.67%) and High grade squamous intraepithelial lesion (HSIL) in 1 (3.33%) subjects. The cytological features of HSIL (Figure 1), LSIL (Figure 2), ASC-H (Figure 3), AGC-NOS (Figure 4) and ACSUS (Figure 5) are shown respectively.
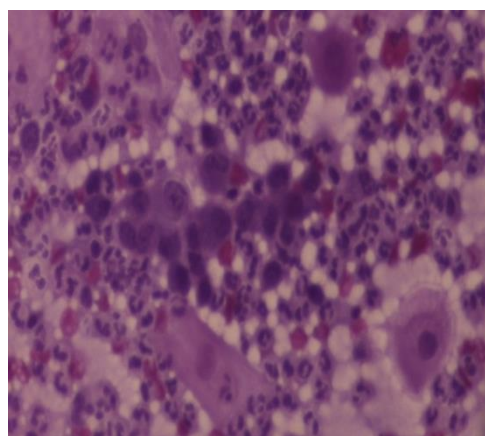

Figure 1: HSIL: Small cells with nucleomegaly more than 2/3rd of the cell with irregular nuclear borders and coarse chromatin. Inflammatory cells in the background. No necrosis (Pap 400x).
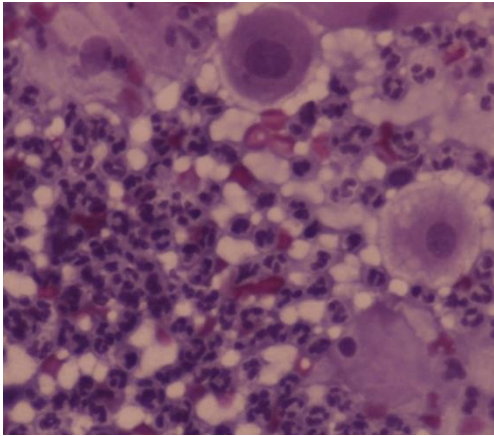
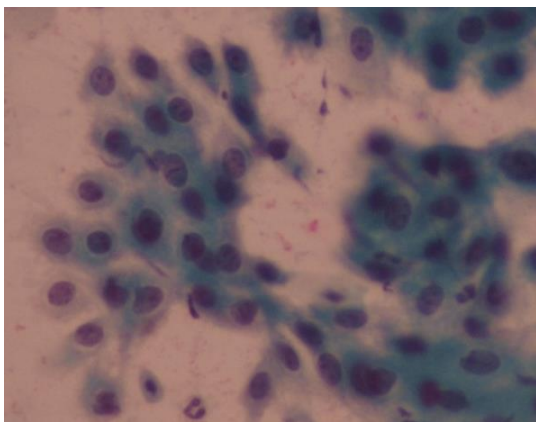**Figure 2: LSIL: Nucleomegaly, nucleus less than 1/2 of the cell area (Pap 400x).**

Figure 3: ASC-H: Squamous cells with nucleomegaly more than 2/3rd of the cell with coarse chromatin and regular nuclear borders (Pap 400x).
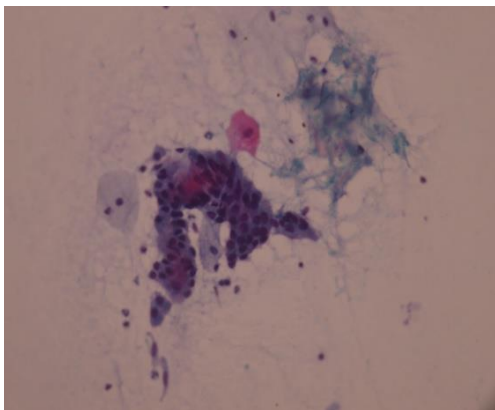

Figure 4: AGC NOS: sheets of endocervical cells with nucleomegaly (Pap 100x).

Among the Negative for intraepithelial lesions (NIEL) cases, non-specific infections were seen in 131 (84%) subjects, specific infections in 25 (16%) of subjects. Candida species infection was the most common comprising 12.82% of cases, followed by Trichomonas (1.3%) and a co infection of both was seen in 1.92%.
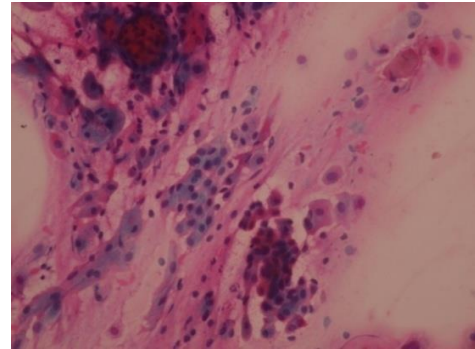

Figure 5: ASC - US: Nucleomegaly more than half of the cell with regular nuclear membrane and fine chromatin (Pap 100x).

Among the 30 women with ECA, 13were asymptomatic. Out of the remaining 17 symptomatic subjects, 9 presented with menstrual irregularities, 6 with white discharge and 2 with bleeding on touch (Table 1). Ten out of the 30 subjects with ECA had a healthy appearance of cervix on clinical examination. Visual inspection with acetic acid (VIA) test was positive in 16 out of the 30 subjects with ECA. In the decreasing order, ECA occurred at proportions of 30%, 26.67%, 23.33%, 16.67%, and 3.33% in 40-49 years, 30-39 years, 50-59 years, 20-29 years and 60-69 years age groups respectively (Table 2). Therefore ECA were more common in the 30-60 years age group (80%). Among all the women with ECAs, 63.3% were married between 13-18 years of age. Nearly 60% (18 in number) of the women had their first child birth before an age of 19 years with 56.7% with age at first child birth between 15-19 years. While 53.3% (majority) were in the parity range of 1-2, a proportion of 43.3% women were in the 3-4 parity range. 30% (9 in number) of the women with ECAs were illiterate. In the present study, none of the women were aware of the Pap screening test. The prevalence of ECA with respect to age groups affected (Table 2), age at marriage (Table 3), age at childbirth (Table 4), parity (Table 5), and educational status of the women (Table 6), are shown respectively.

DISCUSSION

Women in India face constraints not only in obtaining health services, but also in expressing reproductive health needs. Lack of awareness, cultural barriers and economic factors prevent them from seeking timely care. In the present study, none of the women were aware of the Pap screening test. In this setting a regular Pap screening programme is very much essential to study the pathological changes of the cervix.

In the present study, majority of the women were in 20-59 years age group (97.9%). Negative for intraepithelial lesions (NIEL) were found in 156 (83.9%) and epithelial cell abnormalities (ECA) were seen in 30 (16.1%). Among the NIEL subjects, non specific infections were seen in 131 (84%) and specific infections in 25 (16%).

Table 1: Clinical characteristics of subjects with epithelial cell abnormality.

Clinical characteristics	ECA Total (%)	ASC-US (%)	ASC-H (%)	LSIL (%)	HSIL (%)	AGC-NOS (%)
Asymptomatic	13 (43.3%)	9 (45%)	-	3 (60%)	1 (100%)	-
Menstrual abnormalities	9 (30%)	7 (35%)	-	1 (20%)	-	1 (50%)
White discharge	6 (20%)	2 (10%)	2 (10%)	1 (20%)	-	1 (50%)
Bleeding on touch	2 (6.7%)	2 (10%)	-	-	-	-

Table 2: Epithelial cell abnormalities in subjects in relation with age.

Age group (yrs)	ECA Total N=30 (%)	ASCUS N=20 (%)	ASC-H N=2 (%)	LSIL N=5 (%)	HSIL N=1 (%)	AGC-NOS N=2 (%)
20-29	5 (16.67%)	1 (5%)	1 (50%)	1 (20%)	-	2 (100%)
30-39	8 (26.67%)	6 (30%)	-	2 (40%)	-	-
40-49	9 (30.0%)	9 (45%)	-	-	-	-
50-59	7 (23.33%)	3 (15%)	1 (50%)	2 (40%)	1 (100%)	-
60-69	1 (3.33%)	1 (5%)	-	-	-	-

Table 3: Epithelial cell abnormalities in subjects in relation with age at marriage.

Age group (yrs)	ECA Total N=30 (%)	ASC-US N=20 (%)	ASC-H N=2 (%)	LSIL N=5 (%)	HSIL N=1 (%)	AGC-NOS N=2(%)
<13	1	1(5%)	-	-	-	-
13-18	19(63.3%)	14(70%)	1(50%)	3(60%)	-	1(50%)
≥19	10(33.3%)	5(25%)	1(50%)	2(40%)	1(100%)	1(50%)

Table 4: Epithelial cell abnormalities in subjects in relation with age at first child birth.

Age group (yrs)	ECA Total N=30 (%)	ASCUS N=20 (%)	ASC-H N=2 (%)	LSIL N=5 (%)	HSIL N=1 (%)	AGC-NOS N=2 (%)
≤14	1 (3.3%)	1 (5%)	-	-	-	-
15-19	17 (56.6%)	14 (70%)	1 (50%)	2 (40%)	-	-
20-24	11 (36.6%)	4(20%)	1 (50%)	3 (60%)	1 (100%)	2 (100%)
25-29	1 (3.3%)	1 (5%)	-	-	-	-

Table 5: Epithelial cell abnormalities in subjects in relation with parity.

Parity	ECA					
	Total N=30 (%)	ASCUS N=20 (%)	ASC-H N=2 (%)	LSIL N=5 (%)	HSIL N=1 (%)	AGC-NOS N=2 (%)
1-2	16 (53.3%)	10 (50%)	-	4 (80%)	-	2 (100%)
3-4	13 (43.3%)	9 (45%)	2 (100%)	1 (20%)	1 (100%)	-
≥5	1 (3.3%)	1 (5%)	-	-	-	-

Table 6: Epithelial cell abnormalities in subjects in relation with educational status.

Literacy	ECA					
	Total N=30 (%)	ASCUS N=20 (%)	ASC-H N=2 (%)	LSIL N=5 (%)	HSIL N=1 (%)	AGC-NOS N=2 (%)
Illiterate	9 (30.0%)	7 (35%)	-	2 (40%)	-	-
Primary	4 (13.3%)	4 (20%)	-	-	-	-
Intermediate	13 (43.3%)	7 (35%)	2 (100%)	2 (40%)	1 (100%)	1 (50%)
Higher	4 (13.3%)	2 (10%)	-	1 (20%)	-	1 (50%)

When the 30 subjects with ECA were studied, the prevalence of the epithelial cell abnormalities was more common in women aged between 30-60 years (80%) being highest in the 40-49 year age group (30%). ECA were also found to be more common in those who were married between 13-18 years of age (63.3%) and in those with age at first child birth between 15-19 years (567%). Most of the women with ECA (53.3%) were in the 1-2 parity range. Majority (75%) of the ASCUS were identified in women in the age group of 30-49 years. LSIL were equally distributed in the 30-39 years and 50-59 years age group. The two subjects with AGC-NOS were in the 20-29 years age group. The single case of HSIL occurred in a woman aged 50 years. The ages of the two subjects with ASC-H were 26 years and 56 years (Table 2). No malignancies were detected in our study.

Our study reports a higher prevalence of ECA. In a study conducted by Urmila Banik et al.[8] 53.96% of subjects were in 20-44 years age group, 8.18% revealed ECA which showed a bimodal age distribution with majority aged 45 years or above; and high grade lesions and malignancy were found to be more common in women belonging to the 30-39 and ≥45 age groups. In our study, smears in 16.1% revealed ECA and 56.7% of them were aged above 40 years. In a screening programme for women at the largest urban slum in Asia at Dharavi, Mumbai,[9] out of 164 women screened, the Pap smear reports showed ECA in 2.44% of subjects. NIEL with nonspecific infections were seen in 59.7% and specific infections were seen in 8.54% of the subjects. The results

in this study are compared with results from our study, shown in Table 7. In a community based cervical cancer screening programme for women, conducted by Maulana Azad Medical College, New Delhi,[10] screening was done in 435 women who attended the camp, of which 95.7% were in the reproductive age group (15-44years) and 64.4% were illiterate. It was observed in their study, that 53.3% of the women had at least one but less than three children. Most (82.53%) of the women attending the camp had a family income of more than 1000rupees per month. Among the 13 women with ECA (CIS and high grade carcinoma), majority were married at an age <18 years, had given birth to >3 children and were illiterate. The results are compared with results from our study, shown in Table 8. The observed difference in prevalence of ECA among subjects in various studies may be attributed to the differences in setting, geographical variation or methodology used.

Table 7: Comparison of the results from present study with other similar studies.

Characteristics	Dharavi study	Our study
Total number of subjects	164	186
NIEL (non-specific infections)	59.76%	70.4%
NIEL (specific infection)	8.54%	13.44%
Epithelial cell abnormality	2.44%	16.1%

Table 8: Comparison of the results from present study with other similar studies.

Characteristics	Maulana Azad Medical College study	Our study
Total number of subjects	435	186
Illiterate	64.4%	24.7%
Family income >1000 rupees	82.53%	100%
Age at marriage <18 years	31.45%	51.6%
Parity: 1-2	53.3%	70.4%
Non-specific changes	41.1%	70.4%
Specific infection	23.4%	13.44%

CONCLUSION

In the present study epithelial cell abnormalities were found to be more common in women in the age group of 30-60 years (80%), with age at marriage between 13-18 years (63.3%), with age at first child birth between 15-19 years (56.7%). This signifies that these women are among the poor users of cytological screening programme. The findings of the study highlight the utility and need of Pap screening at regular intervals through camp based approach in the community.

REFERENCES

1. Government of India - World Health Organization Collaborative Programme 2004-2005. Guidelines for cervical cancer screening programme; 2006. Available at: http://www.cytoindia.com/ cytologyeqa/ ccsp. gudelines.pdf.
2. Manjit Singh Bal, RishuGoyal, Anil Kumar Suri, Manjit Kaur Mohi. Detection of abnormal cervical cytology in Papanicolaou smears. J Cytol. 2012;29(1):45-7.
3. Veena Kashyap, Suresh Hedau, Suresh Bhambhani. Defining the validity of classical andnon-classical cellular changes indicative of low-grade squamous intraepithelial lesion encompassing human papillomavirus infection in relation to human papillomavirus deoxyribonucleic acid testing. J Cytol. 2011;28(4):159-64.
4. Kerkar RA, Kulkarni YV. Screening for cervical cancer: An overview. J Obstet Gynaecol India 2006;56:115-22.
5. Afrakhteh M, Khodakarami N, Moradi A, Alavi E, Shirazi FH. A study of 13315 Papanicolaousmear diagnoses in Sohada hospital. J Fam Reprod Health 2007;1:75-9.
6. Sankaranarayanan R, Budukh A, Rajkumar R. Effective screening programs for cervical cancer in low- and middle- income developing countries. Bull World Health Organ 2001;79:954-62.
7. Nandakumar A, Ramnath T, Chaturvedi M. The magnitude of cancer cervix in India. Indian J Med Res 2009;130:219-21.
8. Urmila Banik, Pradip Bhattacharjee, Shahab Uddin Ahamad, Zillur Rahman. Pattern of epithelial cell abnormality in Pap smear: A clinicopathological and demographic correlation. Cyto Journal 2011;8:8.
9. D. Pandit, R. Prabha, S. Shanbhag, R. Mayekar. Morbidity Pattern of Women Attending Screening Program in an Urban Slum in Mumbai. Indian J Community Med 2005;30(4):134-5.
10. Pragya Sharma, Manju Rahi, Panna Lal. A community-based cervical cancer screening Program among women of Delhi using camp approach. Indian J Community Med 2010;35:86-8.