

Pap smear study of health insured patients covered under employees' insurance scheme in a tertiary care hospital

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Abstract

Background: Cancer of the cervix is a leading cause of morbidity and mortality among women worldwide. Papanicolaou smear test is the best screening method for detecting premalignant lesions and to diagnose cervical cancer.

Objectives: The objective of the study was to find out the distribution of abnormal Pap smears in our hospital which caters to the low socio-economic group with health insurance cover. To evaluate the effectiveness of Pap smears in population with access to health care.

Materials and Method: An analysis of 9189 Pap smears received in the department of Pathology as a part of routine clinical work up and screening protocol from January 2012 to July 2016 were taken. Comparison of our data with other population based studies world over was carried out.

Results: The mean age of the patients was 40.18±9.7 years. Most of them were of age group 31-40 years (38.1%), followed by 41-50 years (32.3%), 21-30 years (17.2%), 51-60 years (9.1%), >60 years (3.1%) and <20 years (0.2%). A total of 8,939 (97.3%) samples were adequate for evaluation whereas 250 (2.7%) samples were inadequate for opinion. Of 8,939 smears, 8585 smears (96.4%) were negative for intraepithelial lesions and 236 smears (2.64%) showed epithelial cell abnormalities. The 236 cases included ASC-US (1.12%), ASC-H (0.05%), LSIL (0.50%), HSIL (0.85%), Squamous cell carcinoma (0.09%) and AGC (0.01%). Three sixty three Pap smears (negative smears 272, positive smears 91) had corresponding punch biopsy and hysterectomy specimens for cyto-histology correlation study. The sensitivity of Pap smear in our study was 68.5%, specificity was 94.89%, positive predictive value of 81.3% and Negative Predictive value of 90.27% and Diagnostic accuracy of 88.4%.

Conclusion: Pap smear is a screening tool for early detection of precancerous lesion and prevents cancer as there is a long latent phase before they progress to frank malignancy. The prevalence of abnormal pap smears in our study correlated with the other studies in India. Our patients though belong to lower socioeconomic group; they are covered under health insurance scheme and have access to the health care facility. However public awareness regarding the utility of this test should be enhanced so that more women will benefit.

Keywords: Papanicolaou Smear (PAP), Screening, Epithelial Cell Abnormalities.

Introduction

Cervical cancer is the leading cause of morbidity and mortality in women worldwide. Developing countries constitute eighty percent of the global disease burden.⁽¹⁾ As per the data from GLOBOCAN 2012, the top three malignancies in women are breast, cervix and colorectum.⁽²⁾ According to the National cancer registry programme (NCRP) data of Indian Council of Medical Research there is a wide demographic variation in the incidence of cancer. According to the report from Chennai, the leading cancer sites among women were breast (30.7%) followed by cervix uteri (12.6%), ovary (6.6%), corpus uteri (4.6%) and stomach (4.1%).⁽³⁾ Effective screening programme in developed countries have substantially reduced the incidence of cervical cancer and mortality rates.^(4,5) The average cervical cancer screening coverage in developed countries is 63%, whereas in developing countries it is only 19%.⁽⁴⁾ Various screening methods used are Visual inspection of the cervix with application of diluted acetic acid and Lugol's iodine, Visual inspection with magnifying device, the Pap smear study and HPV testing with high risk probe of Hybrid capture 2 assays.⁽⁶⁾ Pap smear serves as an excellent screening tool in view of the cost

effectiveness, easy accessibility of the cervix to colposcopic examination, long latency of precancerous lesions. Even though sensitivity and specificity of Pap smear is not high, it is still the commonly used screening method.⁽⁶⁾ The present study was carried out to assess the prevalence of abnormal pap smears in a tertiary care hospital for insured patients of low socioeconomic status.

Materials and Method

Cases were collected from the archives of Department of Pathology from January 2012 to June 2016. Our patients belong to low socioeconomic group with access to medical facility under the Employees' state insurance scheme. The study included 9189 conventional pap smears, classified according to The Bethesda system (TBS) 2001. The results were analysed by descriptive statistical analysis using SPSS version 20.

Results

A total of 9189 pap smears were analysed. Mean age of the patients was 40.18±9.7 years (ranging from 16 years to 85 years). Most of them were of age group 31-40 years (38.1%), followed by 41-50 years (32.3%), 21-

30 years (17.2%), 51-60 years (9.1%), >60 years (3.1%) and <20 years (0.2%) (Fig.1). A total of 250 (2.7%) samples were inadequate due to low cellularity and inflammatory cells and blood obscuring the cells. Majority of inadequate smears belong to patients with history of mass descending per vagina.

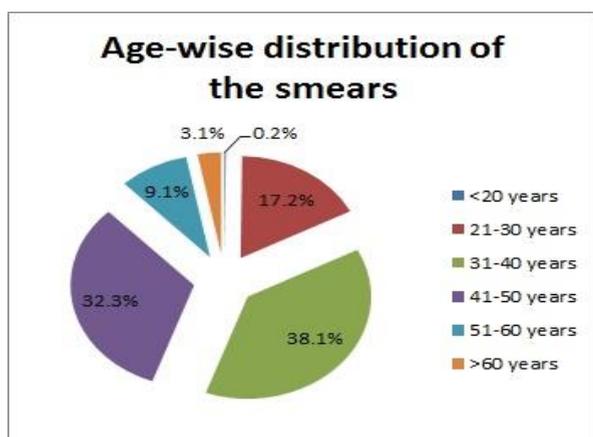


Fig. 1: Age-wise distribution of smears

Of 8,939 smears, 8585 smears (96.4%) were negative for intraepithelial lesion/ malignancy (NILM) (Table 1) and 236 smears (2.64%) showed epithelial cell

abnormalities. Epithelial cell abnormalities included atypical squamous cells of undetermined significance (ASC-US 1.12%), atypical squamous cells cannot exclude HSIL (ASC-H 0.05%), Low grade squamous intraepithelial lesion (LSIL 0.50%), High grade squamous intraepithelial lesion (HSIL 0.85%), squamous cell carcinoma (0.09%) and Atypical glandular cells (0.01%). The ASC/SIL ratio was 0.87 (Table 2). Age distribution of the patients with epithelial cell abnormalities was given in (Table 2).

Table 1: Categorisation of Negative smears

Negative for Intraepithelial lesion/malignancy	8585	96.04%
Normal	2269	25.38%
Atrophy	345	3.86%
Inflammatory smears	5971	66.80%
Inflammation NOS	3454	38.63%
Specific infection	2385	26.69%
Bacterial vaginosis	1331	14.9%
Trichomonas vaginalis	98	1.10%
Candida	955	10.68%
Herpes	1	0.01%
Reactive cellular changes	133	1.49%

Table 2: Categorisation of smears with epithelial cell abnormalities

Type of abnormality	No. of cases	Overall percentage	Age distribution					
			0-20 Years	21-30 Years	31-40 Years	41-50 Years	51-60 Years	>60 Years
ASCUS	100	1.12%	0	6	17	49	19	9
ASCH	5	0.055	0	0	1	3	1	0
LSIL	45	0.50	0	5	8	20	10	2
HSIL	76	0.85	0	3	23	34	12	4
SCC	8	0.09	0	0	0	2	3	3
AGC	1	0.01	0	0	1	0	0	0
Positive for malignancy	1	0.01	0	0	0	0	1	0
Total cases	236	2.64%						
ASC/ SIL ratio: 0.87								

Vault smear following hysterectomy constituted 118 cases (1.32%), of which 88 cases (0.98%) were normal, 28 cases (0.31%) showed radiation changes and 2 (0.02%) cases showed atypia.

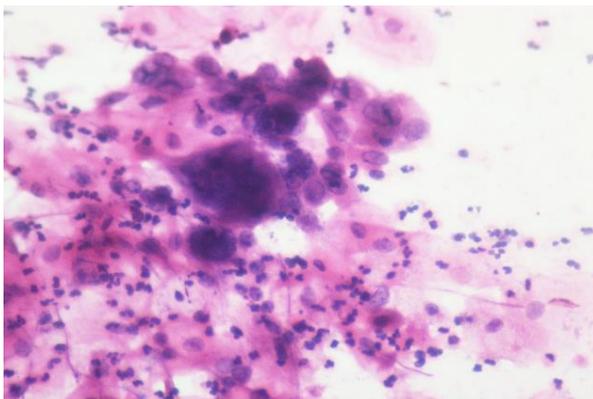
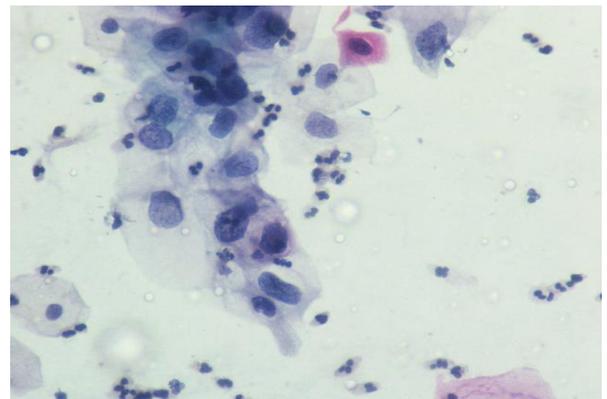
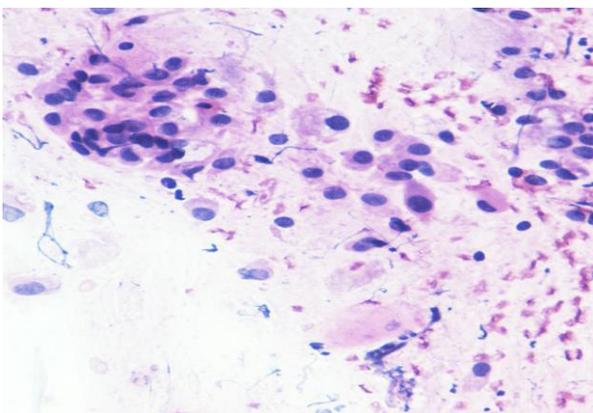
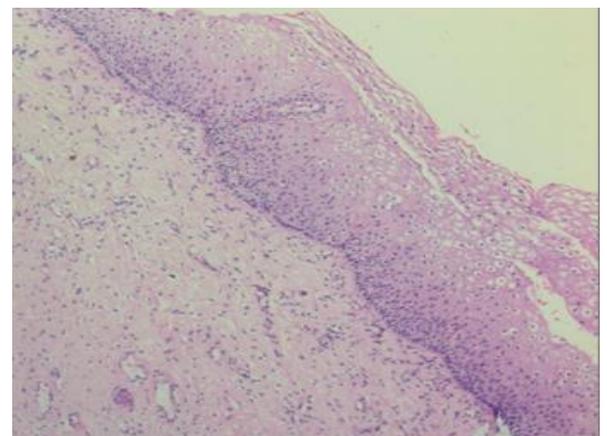
Three sixty three Pap smears (negative smears 272, positive smears 91) had corresponding punch biopsy or hysterectomy specimens for cyto-histology correlation study (Table 3). 321 pap smears correlated with the biopsy findings and 42 smears showed discrepancies (Table 4) (Fig. 2-6). The sensitivity of Pap smear in our study was 68.5%, specificity was 94.89%, positive predictive value of 81.3% and Negative Predictive value of 90.27% and Diagnostic accuracy of 88.4%.

Table 3: Cyto-histopathological correlation: 363

Cytological patterns on pap smears	Number of cases on pap smears	Histopathological diagnosis					
		Non neoplastic	CIN I	CIN II	CIN III	CIS	SCC
Negative	272	260	6	-	3	-	3
ASCUS	25	10	11	-	-	2	2
ASCH	2	-	-	-	-	1	1
LSIL	20	1	17	2	-	-	-
HSIL	38	-	3	12	13	1	9
SCC	6	-	-	-	-	-	6
Total	363	271	37	14	16	4	21

Table 4: Correlated and non-correlated cases on histopathology (N=363)

Cytological patterns on pap smears	Number of cases on pap smears	Correlated	Non-correlated
Negative for intraepithelial lesion or malignancy(NILM)	272	260	12
Epithelial cell Abnormality	91	61	30
ASCUS	25	11	14
ASCH	2	1	1
Premalignant (LSIL& HSIL)	58	43	15
SCC	6	6	0

**Fig. 2: Microphotograph shows cellular changes of Herpes virus infection. (H&E, X400)****Fig. 4: (A) Microphotograph shows features of LSIL. (Pap stain, X400)****Fig. 3: Microphotograph shows atypical squamous cells of undetermined significance (H&E, X400)****Fig. 4: (B) Corresponding biopsy showing CIN I (H&E, X40)**

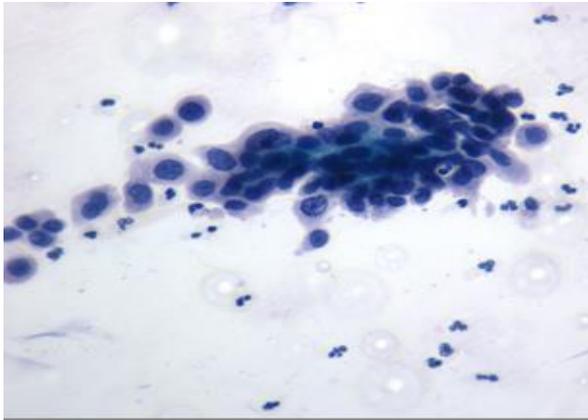


Fig. 5: (A) Microphotograph shows features of HSIL. (Pap stain, X400)

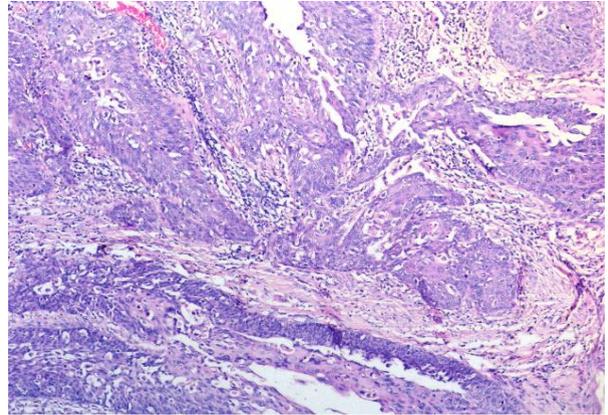


Fig. 6: (B) Corresponding biopsy showing moderately differentiated squamous cell carcinoma (H&E, X40)

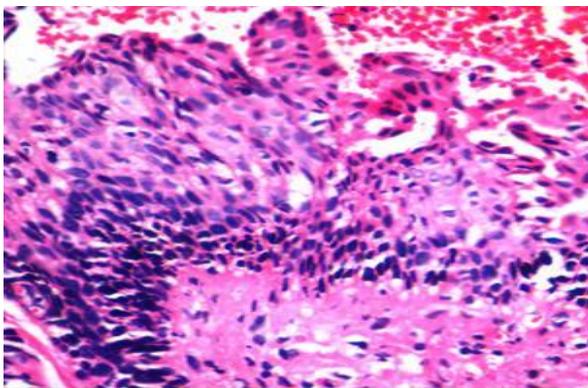


Fig. 5: (B) Corresponding biopsy showing CIN III with Carcinoma in situ changes (H&E, X40)

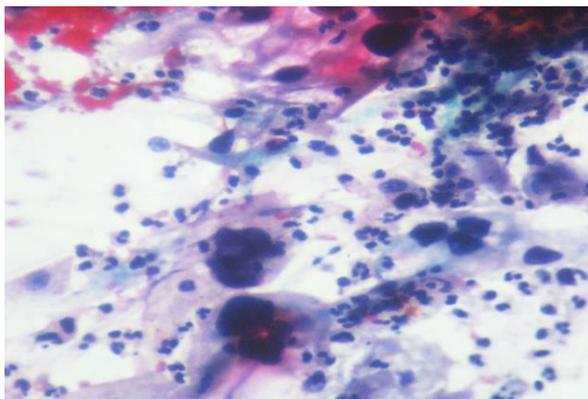


Fig. 6: (A) Microphotograph shows features of squamous cell carcinoma. (Pap stain, X400)

Discussion

Cervical cancer ranks third among all malignancy in women worldwide.⁽¹⁾ One fifth of all new cases are reported in India.⁽⁶⁾ Risks expressed as lifetime risk (0-64 years) for development of cervical cancer was one out of every 25 in the year 1982 with a decrease to one out of every 68 in the year 2008 in Chennai.⁽⁷⁾ However in rural areas the trend remains the same⁽⁸⁾ due to several risk factors like early marriage, early age at first coitus, multiparity and low socioeconomic status.⁽⁹⁾ This mandates the need for a widespread screening programme to reduce the burden considerably. The WHO recommends that in developing countries, women aged 18-69 years should be screened for cervical cancer every 3 years.⁽¹⁰⁾ In India it is mainly an opportunistic screening with coverage of 2.6 to 5%.⁽⁶⁾ In our study, the age group of patients ranged from 16 to 85 years. Similar distribution of age was seen in the studies by Kalyani et al (17-88 years)⁽⁶⁾ and Banik U et al (15-82 years).⁽¹¹⁾

Unsatisfactory specimens require considerable time and effort as it was found in a study that unsatisfactory smears were more often from high risk patients and a significant number of these were followed by SIL/cancer when compared to satisfactory specimens.⁽¹²⁾ Percentage of unsatisfactory smears in our study was not high (2.7%), whereas in other studies it ranged from 0.73% to 17.8% (Table 5).^(1,6,9,13,14,15)

Non-specific inflammation formed 38.63% and specific infection (candida, trichomonas, bacterial vaginosis and Herpes infection) formed 26.69% in our study, whereas in the urban population based study by Mulay et al was 19.61% and 6.07% respectively.⁽¹³⁾ Both specific and non-specific infections were higher in our study, probably due to our patients belonging to lower socioeconomic group.

Abnormal Pap smears in our study constituted 2.64% of cases whereas in other Indian studies it ranged from 1.392% to 27.5% (Table 5). The percentage of abnormal smears in the study by Velu AR et al on postmenopausal women conducted in the rural tertiary

care centre was 17.8%, of which 12.7% of the patients were asymptomatic.⁽¹⁶⁾ The prevalence of epithelial abnormalities was higher in the rural population and low socioeconomic group, when compared to the study on urban affluent population (Table 5). Wide range of prevalence of epithelial cell abnormality has been reported in other countries with 8.18% in Bangladesh,⁽¹¹⁾ 0.47% in Mauritius,⁽¹³⁾ 1.7% in Nepal,⁽¹⁷⁾ 3.12% in china (conventional method),⁽¹⁸⁾ 17.3% in Western Saudi Arabia,⁽¹⁹⁾ 4.43% in Kuwait,⁽²⁰⁾ 14.1% in Northwest Ethiopia⁽²¹⁾ and 3.7% in Belgium⁽²²⁾ (Table 6). The variations can be attributed to sample size and duration of the study, referral/ tertiary care centre, ethnicity of the study population, risk factors, socioeconomic status and inclusion criteria used in the studies. The age group of the patients with premalignant lesion of the cervix in our study was 27-70 years and squamous cell carcinoma was 44-76 years which in comparison to the study by Kalyani et al was 30-59 years and 47 to 65 years respectively.⁽⁶⁾

Though our patients belong to lower socioeconomic group, the epithelial abnormalities are picked up earlier, as they have improved and free access to health care facilities. The percentage of ASCUS, LSIL, HSIL and SCC in our study was 1.12%, 0.5%, 0.85% and 0.09% respectively. ASCUS was the common epithelial abnormalities noted in most of the studies.^(6,13,14,18-23) ASC/SIL+ ratio, a quality indicator used for assessing screening efficacy was 0.87%. This is within the 5th and 95th percentile reporting rates as given by the guidelines.⁽²⁴⁾ The percentage of HSIL and SCC in our study was below 1% which is comparable with most of the studies except for studies from referral centres like Alta et al (HSIL 3.684%),⁽¹⁾ Nandwani RR et al (HSIL 2.77%, SCC-3.48%),⁽¹⁴⁾ Banik U et al (HSIL 1.18%)⁽¹¹⁾ and Getinet et al (HSIL 4.1%)⁽²¹⁾ (Table 5,6). The study by Getinet et al included high number of HIV infected women, which is one of the independent risk factors for precancerous lesions and cervical carcinoma.⁽²¹⁾

Table 5: Comparison of our study with other Indian studies

Authors	Our study	Alta et al ⁽¹⁾	Kalyani et al ⁽⁶⁾	Gupta K et al ⁽⁹⁾	Mulay et al ⁽¹³⁾	Nandwani RR et al ⁽¹⁴⁾	Geethu G. Nair et al ⁽¹⁵⁾
Study population	Urban and semi-urban	Rural, tribal and semi-urban	Semi-urban & rural	-	Urban	-	-
Place	Chennai	Andhra Pradesh	Bangalore	Western Uttar Pradesh	Hyderabad	Madhya Pradesh	Kerala
Sample size	9189	380	1501	4703	6010	5813	2028
Unsatisfactory smears	2.7%	6.31%	17.8%	13.94%	0.73%	5.73%	2.71%
Major group of the patients	31-40 years (38.1%)	-	30-39 years (32.06%)	30-39 years (40.37%)	41-50 years (33.64%)	30-39 years (45.07%)	-
Percentage of epithelial cell abnormality	2.64% (236)	27.5%(98)	3.08% (38)	3.23%	1.392% (85)	13.12%	2.41% (49)
ASCUS	1.12%	7.894%	1.46%	0.52%	0.64%	3.61%	0.15%
ASC-H	0.055%	-	0.32%	0.05%	-	-	-
LSIL	0.50%	13.157%	0.24%	1.36%	0.216%	2.59%	1.58%
HSIL	0.85%	3.684%	0.41%	0.91%	0.16%	2.77%	0.49%
SCC	0.09%	0.526%	0.41%	0.28%	0.06%	3.48%	0.20%

Table 6: Comparison of our study with studies of other countries

Authors	Our study	Banik U et al ⁽¹¹⁾	Mulay et al ⁽¹³⁾	Ranabhat SK et al, ⁽¹⁷⁾	Deshou H et al ⁽¹⁸⁾	Altaf FJ et al ⁽¹⁹⁾	Kapila K ⁽²⁰⁾	Getinet M et al ⁽²¹⁾	Arbyn M et al ⁽²²⁾
Place	India	Bangladesh	Mauritius	Mid-Western Nepal	China	Western Saudi Arabia	Kuwait	Northwest Ethiopia	Belgium
Sample size	9189	1699	10000	880	31500	7297	140404	391	600000
Percentage of epithelial cell abnormality	2.64%	8.18%	0.47%	1.7%	3.12%	17.3%	4.43%	14.1%	3.7%
ASCUS	1.12%	0.18%	0.26%	0.23%	2.3%	9.3%	2.37%	5.1%	2.2%
ASC-H	0.055%	-	-	-	0.06%	0.8%		-	-
LSIL	0.50%	6.36%	0.07%	0.34%	0.41%	2.7%	0.97%	3.8%	1.1%
HSIL	0.85%	1.18%	0.08%	0.68%	0.28%	0.9%	0.22%	4.1%	0.4%
SCC	0.09%	0.35%*	0.01%	0.23%	0.06%	0.06%	0.09%	1.0%	

*Squamous cell carcinoma and Adenocarcinoma

In the present study out of 25 cases diagnosed as ASCUS on cytology, 11 were cervical intraepithelial neoplasia I (CIN I), 2 were carcinoma in Situ, 2 were squamous cell carcinoma and 10 were non-neoplastic on histopathology. Atrophic changes, hesitation in reporting LSIL in perimenopausal and postmenopausal women, drying artefact and regenerative changes are some of the reasons behind increased reporting of ASCUS. It was recommended in a study by Fallani et al, that all the patients with ASCUS and LSIL should undergo colposcopic examination and directed punch biopsy wherever indicated.⁽²⁵⁾ Of the twelve cases of negative smears, 6 were CIN I, 3 were CIN III and 3 were squamous cell carcinoma. Of the 20 cases of LSIL, 2 smears showed CIN II changes and 1 was negative smear. The major discrepancies are due to sampling error, fixation/drying artefact. Of the 38 cases of HSIL, 9 were squamous cell carcinoma, 3 were CIN I on histology. Remaining patients were lost to follow up and did not have subsequent colposcopy directed biopsy/hysterectomy in spite of the availability of health care benefits. This mandates the need for increasing the awareness of cancer cervix prevention in our population.

The overall sensitivity of Pap smear in our study was 68.5%. Addition of HPV testing will increase the sensitivity of Pap smear study and also duration of screening procedure. Studies have shown that negative HPV testing has a lower subsequent risk for CIN III and cancer when compared to negative cytology.⁽²⁶⁾

Conclusion

Cancer of cervix is readily preventable, by early detection and appropriate timely treatment of its precursor lesions by simple Pap screening test. The prevalence of epithelial abnormality in our study was 2.64% which is higher compared to the study in urban affluent population. The age of detection of premalignant lesion was 27 years and cancer was 44 years in our study. It is detected earlier in our study group. This probably could be due to the health insurance cover which is definitely beneficial to our study population who belong to lower socioeconomic group. Steps to increase the awareness of cancer cervix prevention and also extend the insurance cover to the population can definitely benefit in bringing down the incidence of carcinoma cervix.

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