Spectrum of lesions in papanicolaou smears: An institutional study

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Abstract
Introduction: Carcinoma Cervix is considered to be leading cancer amongst women. Periodic Papanicolaou Smears (PAP) screening is the simplest way to diagnosed precancerous lesion. Factor such as ignorance, poverty, poorly developed public health care delivery system put women in urban slums at a disadvantage of receiving any health screening activity.

Aim: To know the prevalence of epithelial cell abnormalities of the cervix among the patient of various age groups.

Materials and methods: PAP smear collected during cervical cancer screening at R L Jalappa hospital and research center between January 2018 and June 2018 were retrieved from the laboratory records of hospital. 1596 PAP smear results were collected and analyzed with SPSS version 22.40(2.5%) reports were excluded from analysis.

Results: 1092 cases (68.4%) had normal findings. 11 women required multiple PAP smears examination.

Conclusion: In India, lack of awareness, cultural barriers and economic factors prevent women from obtaining health services. Hence, a regular Pap screening programme is very much essential to detect the pathological changes of the cervix. In this study there were 92 cases (2.04%) of abnormal epithelial lesions. About 62% of the total cases were above 30 years. Here LSIL was most common epithelial lesion followed by HSIL and then ASCUS.

Clinical Significance: Women initiate cervical cancer screening late in their life which could be the reason for higher incidence of cervical epithelial abnormalities in later age groups.

Keywords: Cervical smear, PAP Stain, LSIL

Introduction
Carcinoma cervix is one the most common cancer amongst the Indian women population, particularly affecting the 15-44 years of age.1 Cervical cancer screening using Papanicolaou (PAP) stained cervical smears is one of the most effective way of cervical cancer detection and prevention which has great potential in developing countries like India. However, cervical smear screening has significant rates of false-positive and false negative results.2

In view of this several adjunctive including thin layer cytology, detection of Human Papilloma Virus DNA (HPV DNA) by the Hybrid Capture or polymerase chain reaction tests; evaluation of telomerase repeat activity by the Telomeric Repeat Amplification Protocol (TRAP), Fourier-Transform Infrared (FTIR) Spectroscopy and immune cytochemical detection of p16INK4a protein. However, their prohibitive cost and their requirement for excellent infrastructural facilities, ensured that these new technologist have a very limited availability.3

Although Bethesda System of reporting cervical PAP smears is widely accepted there is lack of uniformity in standardization, identification and documentation regarding various grades of lesions detected during cervical cancer screening leading to poor reproducibility among the diagnostic and clinical fraternities.4

Evaluation of specimen adequacy is considered by many to be the single most important quality assurance component of the Bethesda system. The first two versions of the Bethesda terminology included three categories of adequacy: satisfactory, unsatisfactory, and a “borderline” category initially termed “less than optimal” and then renamed “satisfactory but limited by” in 1991. The 2001 Bethesda system replaced the borderline category with broader and simpler terminology consisting of either satisfactory or unsatisfactory smears.5

Carcinoma cervix is the most common genital tract cancer encountered in developing countries accounting for 30% of world cases, 18% are from India. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease. India has a population of 432.2 million women aged 15 years and older who are at a risk of developing cancer.9 10 Incidence rates vary from 0.1 to 12 per 10,000 pregnancies.11 Cervical cancer is the most common malignancy diagnosed during pregnancy comprising about 70%.

Risk factors for cervical cancers include:
1. Women with low socio-economic status
2. Sexually active at a younger age
3. Poor genital hygiene
4. Malnutrition
5. Use of oral contraceptives

Cervical cancer screening programmes implemented in developed countries over the past fifty years have significantly contributed to the reduction of cancer cervix related deaths. However, high incidence and mortality rates continues in developing countries due to the lack of screening programmes.5

The Pap test has been successful in reducing the incidence of cervical carcinoma by 79% and mortality by 70%.2

Pap test’s main benefit is the early detection of pre neoplastic lesions. Sensitivity of Pap smear is 84.20% and specificity is 62.10%.10
Pap test detects 60-70% of cancer cervix and 70% of endometrial cancer. The Papanicolaou (PAP) smear is the most successful screening test for carcinoma, since its introduction the national death from cervical cancer has dropped by 70%.\(^{11}\)

The accuracy of Pap smear in pregnancy is almost similar to that of non-pregnant women.\(^6\)

Many patients present with advance disease during initial visit to the hospital, due to lack of well-established screening programmes. In rural India, pregnancy and a request for antenatal care may be the only reason for a woman to consult a health professional. Most cervical abnormalities in pregnancy are discovered as a result of routine screening at the initiation of prenatal care.\(^7,\)^\(^8\)

Hence screening by Pap smear during pregnancy useful to screen more number of women in reproductive age group, offers unique and efficient way to detect early cervical changers and hence take timely action.\(^12\)

Even though Pap smear and its efficacy as a screening aid for cervical cancer has been extensively studies over decades, studies which are done during pregnancy are not many.

**Aims**

1. To study the incidence of cervical smears abnormalities.
2. To analysis the various cervical epithelial lesions detected by PAP smear.
3. To determine the cytological –histological correlation among the various cervical lesion detected.

**Materials and Methods**

**Source of Data:** Total of 1596 antenatal women who have visited to OPD of Department of Obstetrics and Gynecology at R.L.Jalappa and Research Centre constituent of Sri Devaraj Urs Medical College, Tamaka, Kolar from January 2018 to June 2018 were included in my study. Institutional ethical clearance certificate was obtained before start of study.

**Study Design:** Cross- sectional descriptive study

**Study Period:** 6 months

**Inclusion Criteria**

All Antenatal women of 14 weeks to 40 weeks of gestational age attending outpatient department for antenatal care at Sri R.L. Jalappa Hospital and Research Centre during the study period.

**Exclusion Criteria**

1. Who have been previously diagnosed with cervical pathology
2. With unexplained vaginal bleeding
3. In established labor
4. Having history of recent coitus or using any vaginal medications.

**Materials**

1. Vaginal speculum
2. Wooden Ayer’s spatula
3. Clean glass slides
4. Fixative containing 95% ethyl alcohol
5. Cotton swab

Pap smears were made by conventional Pap smear techniques, following visual checking 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.\(^4\)

**Results**

The mean age of the women was 45.77±10 years was considered as mean age of women.Normal PAP smear was seen in 1092 (70.18%) women. Multiple PAP smear was done for 11 cases the results were as follows: ASCUS 10(0.64%), Inflammatory 372 (23.91%), LSIL 52 (3.34%), ASC-H 8(0.5), AGUS 2(0.13%) and HSIL 18(1.16%) were reported in women, respectively. Squamous cell carcinoma was reported in 2 (0.13%) women. (Refer Table 1). The incidence of various epithelial cell abnormalities in different age groups are represented in Table 2.

**Table 1: Various lesions of cervix**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>NILM</td>
<td>1092</td>
<td>70.18%</td>
</tr>
<tr>
<td>INFLAMMATORY</td>
<td>372</td>
<td>23.91%</td>
</tr>
<tr>
<td>LSIL</td>
<td>52</td>
<td>3.34%</td>
</tr>
<tr>
<td>ASCUS</td>
<td>10</td>
<td>0.64%</td>
</tr>
<tr>
<td>HSIL</td>
<td>18</td>
<td>1.16%</td>
</tr>
<tr>
<td>ASC-H</td>
<td>8</td>
<td>0.51%</td>
</tr>
<tr>
<td>AGUS</td>
<td>2</td>
<td>0.13%</td>
</tr>
<tr>
<td>SCC</td>
<td>2</td>
<td>0.13%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1556</strong></td>
<td><strong>100.00 %</strong></td>
</tr>
</tbody>
</table>
Table 2: Age wise distribution of various lesions of cervix

<table>
<thead>
<tr>
<th>Age Group</th>
<th>NILM</th>
<th>Inflammatory</th>
<th>LSIL</th>
<th>ASCUS</th>
<th>HSIL</th>
<th>ASC-H</th>
<th>AGUS</th>
<th>SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>24(2.2%)</td>
<td>20(5.4%)</td>
<td>4(7.7%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>21-30</td>
<td>455(21.66%)</td>
<td>75(20.25)</td>
<td>13(25%)</td>
<td>0(0.0%)</td>
<td>1(5.6%)</td>
<td>0(0.0%)</td>
<td>1(50.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>31-40</td>
<td>373(34.16%)</td>
<td>165(44.3%)</td>
<td>14(27%)</td>
<td>3(30%)</td>
<td>4(22.2%)</td>
<td>2(25.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>41-50</td>
<td>154(14.1%)</td>
<td>81(21.8%)</td>
<td>17(32.7%)</td>
<td>5(50%)</td>
<td>6(33.3%)</td>
<td>3(37.5%)</td>
<td>1(50.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>51-60</td>
<td>69(6.32%)</td>
<td>28(7.5%)</td>
<td>4(7.6%)</td>
<td>2(20%)</td>
<td>5(27.8%)</td>
<td>2(25.0%)</td>
<td>0(0.0%)</td>
<td>1(50.0%)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>17(1.56%)</td>
<td>3(0.8%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>2(11.1%)</td>
<td>1(12.5%)</td>
<td>0(0.0%)</td>
<td>1(50.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>1092(100%)</td>
<td>372(100%)</td>
<td>52(100%)</td>
<td>10(100%)</td>
<td>18(100%)</td>
<td>8(100%)</td>
<td>2(100%)</td>
<td>2(100%)</td>
</tr>
</tbody>
</table>

Table 3: Comparison of overall statistical parameters with other studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity%</th>
<th>Specificity%</th>
<th>PPV %</th>
<th>NPV%</th>
<th>Diagnostic Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saha et al</td>
<td>76</td>
<td>83.3</td>
<td>86.4</td>
<td>71.4</td>
<td>79.1</td>
</tr>
<tr>
<td>Mallur et al</td>
<td>41.66</td>
<td>81.2</td>
<td>86.21</td>
<td>78.26</td>
<td>40</td>
</tr>
<tr>
<td>Jain et al</td>
<td>78</td>
<td>26.9</td>
<td>91</td>
<td>11.3</td>
<td>73.2</td>
</tr>
<tr>
<td>Ashmita et al</td>
<td>19.51</td>
<td>83.3</td>
<td>80</td>
<td>86.5</td>
<td>23.26</td>
</tr>
<tr>
<td>Chaudary et al</td>
<td>25.4</td>
<td>99.27</td>
<td>94.12</td>
<td>74.3</td>
<td>76</td>
</tr>
<tr>
<td>Naik et al</td>
<td>79.4</td>
<td>58.3</td>
<td>86.1</td>
<td>46.6</td>
<td>74.5</td>
</tr>
<tr>
<td>Present study</td>
<td>66.1</td>
<td>99</td>
<td>84.78</td>
<td>97.27</td>
<td>96.53</td>
</tr>
</tbody>
</table>

Fig. 1: PAP Staining of NILM smear [40X]

Fig. 2: PAP Staining of INFLAMMATORY smear [40X]

Fig. 3: PAP Staining of ASCUS smear [40X]

Fig. 4: PAP Staining of LSIL smear [40X]
Discussion

Cancer cervix is both preventable and curable disease. It is preventable by cervical screening and curable if identified at an early stage. Screening cytology and early treatment constitute the sheet anchor of control of the disease. It is the third most common type of gynecological cancer in women world wide. It accounts for 15% of all malignancies in developing countries where women do not have access to cervical cancer screening and prevention programs it remains the second most common type of cancer.14

Indian contribution to cervical cases and mortality is 25.4% and 26.5% respectively. Majority of Indian women diagnosed with this disease have never been screened for this condition. Around 70% present in advanced stages due to absence of an organized cancer screening program.14

According to national cancer institute, strong risk factors include early age at first intercourse, history of multiple sexual partners, genital human papilloma virus infection (HPV) or other sexual transmitted disease (STD), and the presence of history of other genital tract abnormalities. One reason that many of these women do not get screened for cervical cancer is that they often don’t view themselves as being at risk. Available literature shows that women often participate in cervical cancer screening less regularly, leading to lesions that are found in more advanced are less curable stage. Many women do not want to discuss sexual issues due to embarrassment despite appropriate counseling. About 24.1% (33 of 137 women) of the women had early marriages.16

As per one prospective analysis which was conducted on 200 pregnant women to screen for cervical neoplasia and pre-malignant diseases in pregnant women during first antenatal visit who do not have access to routine health care on demographic characteristic, risk factors of cervical cancer and results of Papanicolaou smear. 89.5% of antenatal women had inflammatory smear and 0.5% had LSIL. Risk factors found were multiple sexual partners, extramarital relation of a female, history of HIV and genital warts. The cervical cytology and related education were highly recommended in antenatal women to increase the cervical cancer screening coverage.15

Some studies have compared Papanicolaous test results obtained during pregnancy and post-partum on 1351 pregnant women. Out of these 1351, 1213 underwent Pap test at early pregnancy and post-term. Results to the Pap test were different in 32 patients. Of 1191 patients negative for intraepithelial lesions or malignancy in early pregnancy, 16 had other cytological abnormalities post-term. They performed therapeutic conization post-partum in four patients.17 This study concluded that the results of the Papanicolaou test during pregnancy may not be accurate because of the influence of hormones associated with pregnancy. Taking advantages of one-month post-partum screening visit can lead to early detection of cervical cancer in young people.18

Conclusion

Screening is a new concept introduced in 20th century and comes under secondary prevention. Implementation of appropriate screening method for detection of early disease is especially helpful in cervical cancer as there is a well-defined natural course, long detectable pre-malignant stage, effective treatment modalities to eradicate premalignant lesions and early cervical cancer, easy accessibility of cervix for screening and acceptance of screening tests. Optimal screening method should identify precursors likely to progress to cervical cancer and avoid detection of transient HPV infection and benign lesions.19

Conflicts of Interest: None.

References
