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Evaluation of Cervix at Risk with Pap Smear and with Colposcopy

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Abstract

Background: Unhealthy cervix is a very common finding in Bangladesh due to poor genital hygiene, malnutrition, and multiparity. Cervical Cancer is a serious health problem in Bangladesh and other developing countries. Cervical Cancer is a preventable cancer due to long pre-invasive state and available cervical screening program like pap smear, colposcopy etc. Upon detection the treatment of pre-invasive lesions is highly effective. The objective of our study is to observe and evaluate suspicious cervix upon specimen collection by pap smear and viewing them by colposcopy when required.

Materials and methods: This is a descriptive type of observational cross-sectional study conducted in the Department of Obstetrics and Gynecology of BBMH, Chittagong over a period of six months from December 2020 to June 2021. A total of 64 women were selected, who came to hospital outdoor for the treatment of persistent vaginal discharge, post coital bleeding, post-menopausal bleeding. A thorough general, systemic and pelvic examination was done. Pap smear was conducted and colposcopy was done for women who had persistent inflammation on pap smear cases. Multiple variables like age of marriage and first intercourse, parity contraception was taken in consideration. The data obtained were recorded and statistically analyzed.

Results: Out of 64 women the minimum age was 30 and maximum was 62 years with a mean age of 32.6 ± 7.2 years. Of the 64 women with unhealthy, inflammatory pap smear cases, 33 (51.6%) patients were colposcopically positive for CIN. Then histopathological evaluation of the biopsy material of those 33 women were done. It revealed 12 (36.3%) with abnormal cytology. Patients with positive CIN experienced early marriage, early age of child birth, and also had higher parities than patients without CIN.

Conclusion: This study should that cervical lesion is one of the commonest problems among the females worldwide, including Bangladesh. This revealed the importance of emphasizing on proper screening ofcarcinoma cervix to decline incidence and mortality in developed and developing countries.

Key words : Cervical Carcinoma; CIN; Colposcopy; Pap smear.

Introduction

Cervical Cancer has been the subject of several epidemiological studies since last 150 years. Cancer of the cervix is the second most common life-threatening cancer among women worldwide.[1] It is the second most common cancer after breast carcinoma.

The estimated new cancer cervix cases per year 500,000 of which 79% occur in the developing countries, where it is consistently the leading cancer and there are in excess of 233,000 deaths from the disease.[2] Cancer cervix occupies either the top rank or second among cancers in women in the developing countries, whereas in the affluent countries' cancer cervix does not even find a place in the top 5 leading cancers in women.[3] Although widespread institution of pap smear screening over the last four decades has led to marked reduction in the incidence and mortality, it is still a public health problem.[4] Chronic inflammation either specific or non-specific has been shown to be associated with malignancy and was thought to be one of the factors responsible for carcinogenesis. Persistent inflammation leads to increase cellular turnover specially in epithelium and provides a selection pressure that results in the emergence of cells that are at high risk for malignant transformation.[5] Inflammatory pap smear is the most common record the Gynecologists receives even when the cervix appears normal. The Bethesda system recommends treatment for benign cellular changes on pap smear, screening is initially treatment of infection followed by a repeat pap smear in four to six months' time. If the inflammatory changes continue, the patient is to be subjected to colposcopy.[6]

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However, this is hardly followed, specially in countries like Bangladesh due to lack of awareness and social taboo. Hence, patients do not come to center for screening and remain undiagnosed for years and underwent malignant transformation. The incidence and mortality in the US are about half those for the rest of the world, which is due to part in the success of screening with the papsmear.[7]

The significance of cervical cytology with atypia has been extensively studied. There is a great debate regarding the optimal management of women with persistent inflammatory changes without atypia. While some consider it less likely to be associated with dysplasia, while other recommends farther evaluation due to its association with high incidents of CIN.[8,9] There are few studies that shows the incidents of premalignant and malignant lesions were looked into in cases of inflammatory pap smear. That showed inflammation can obscure few malignant cells and may result in high false negative rates, which may be reduced by employing liquid based cytology.[10] The main reason for this were found to be sampling errors as high as 42.5% being suboptimal and 17.5% being inadequate for interpretation.[11] So, colposcopy of women with inflammatory pap smear may be useful to detect unrecognized cases of CIN. Most women are unaware of the benefit of early screening by speculum examination and pap smear, also social taboo, poverty, ignorance, and inadequate gynecological service at rural area lead to the advancement of the disease. The objective of the study is to see the findings of the cervix at risk and do colposcopy when needed and also to assess the socio demographic and clinical characteristics of patients presenting with unhealthy cervix.

Materials and methods

This is a descriptive type of observational cross-sectional study, which was conducted on 64 women at Department of Obstetrics and Gynecology, Bangabandhu Memorial Hospital (BBMH) Chittagong from December 2020 to June 2021. The patients were given their unique ID and briefed about the objective of the study, risks and benefits, and freedom for participating in the study and confidentiality. Informed written consents were taken and patients were scheduled for their smear tests. Samples were obtained from subjects who ensures to avoid intercourse and lose of any kind of intra vaginal products prior 48 hours of test. Subjects who did not follow the criteria were not involved in the study. Exclusion criteria were patients who were pregnant, menstruating, had a frank growth of surface, and who have undergone hysterectomy. Data have been interpreted and evaluated carefully for statistical conclusion. Ethical clearance was obtained from relevant authority.

The ecto and endocervical samples were obtained by Ayer's spatula and Endocervical cytobrush respectively. Each sample was prepared on glass slide. The slide was fixed immediately with 95% ethanol for 20 minutes. Slides allowed to air dry before sending to the laboratory, were stained by Papanicolaou staining. The slides then studied by the respective pathologist of the hospital. After Pap smear collection, colposcopy was done by using colposcopy machine. After exposing cervix by self-retaining Cusco's speculum, colposcopy examination conducted after cleaning with normal saline. Inspection was done firstly by green filter followed by 3% acetic acid and lugol's iodine application. Margin of lesion, appearance of blood vessels and iodine staining reaction was noted and documented by Reid's score grading system. Punch biopsy was taken if there is colposcopic suspicious area was found and specimen sent for histopathological examination by using Hematoxylin & Eosin stain.

The variables selected were age range, parity, educational status, age of the marriage, age of the first intercourse, contraception, socio economic status, number of sexual partners, personal hygiene, per vaginal discharge, any abnormal bleeding.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, Chicago, IL) version 22.0 software for Windows. Descriptive statistics was performed, and all data was expressed as mean±SD and percentage ratio. The quantitative observations were indicated by frequencies and percentages. Chi-Squared test was used to analyze the categorical variables, shown with cross tabulation. Student t-test was used for continuous variables. p values <0.05 was considered as statistically significant.

Results

64 women were recorded. The minimum age was 30 and maximum was 62 years with a mean age of 32.6±7.2 years (Table I).

Table I Distribution of respondents by their age (n=64)

Age (years)*	Frequency	Percentage (%)
30-40	2	3.1
41-50	31	48.4
51-60	25	39.1
>60	6	9.4

*Mean age = (32.6±7.2) years; Range = (30-62) years

Mean age of the patients at marriage was 14.9 years (Range: 12-23) and the mean age at first child birth was 16.5 years (Range: 13-26) (Table II).

Table II Distribution of respondents by their reproductive life-events (n=64)

Reproductive life-events	Mean±SD	Range
Age at marriage (Yrs)	14.9±1.7	12-23
Age at first child birth (Yrs)	16.5±1.9	13-26

In terms of parity majority (94.5%) of the patients was multipara (Figure 1).

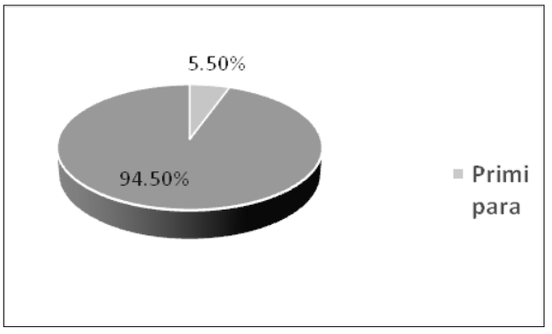

Figure 1 Distribution of respondents by their Parity (n=64)

PAP-smear test reveals bacterial vaginosis and trichomonas vaginalis in 3.1% and 7.8% cases respectively (Table III).

Table III Distribution of subjects by their Pap smear findings (n=64)

Pap smear findings	Frequency	Percentage (%)
Bacterial vaginosis	2	3.1
Trichomonas vaginalis	5	7.8
Thickened	1	1.5

Almost all patients complained of persistent vaginal discharge or leucorrhea not responding to antibiotics (100%). Majority (95.3%) had history of vaginal discharge followed by 71.8% postcoital bleeding and only 37.5% intermenstrual bleeding. Most of the cervixes were broad (78.1%) and cervical erosion was found in 14.0% cases. Nearly 57.8% of uterus was of normal size and 42.1% bulky. Almost all of the uteri exhibited free fornix (Table IV).

Table IV Distribution of subjects by their clinical characteristics (n=64)

Clinical characteristics	Frequency	Percentage (%)
History		
Persistent vaginal discharge	64	100.0
Vaginal discharge	61	95.3
Post-coital bleeding	46	71.8
Intermenstrual bleeding	24	37.5
Per speculum examination		
Cervix		
Broad	50	78.1
Hypertrophy	8	12.5
Normal	6	9.4
Cervical erosion	9	14.0
P/V findings		
Size of uterus		
Bulky	27	42.1
Normal	37	57.8
Fornix		
Free	63	98.4

Discussion

The descriptive type of observational cross-sectional study was carried to see findings of cervix at risk with pap smear and colposcopy were needed. The variables of the study were age range, parity, educational status, age of the marriage, age of the first intercourse, contraception, socio economic status, number of sexual partners, personal hygiene, per vaginal discharge, any abnormal bleeding. A total of 64 patients attending in the Department of Obstetrics and Gynecology during study period were included in the study.

Cervical cancer is a multi-ethology disease and HPV infection alone is not a sufficient cause of cervical cancer.[12] The cofactors such as low socioeconomic status, tobacco smoking, sexual and reproductive factors, HIV and other sexually transmitted diseases, long term contraceptive use, certain micronutrient deficiencies and genetic susceptibility have been suggested.[13]

Ever since cervical pathology, mainly cancer screening with the Papanicolaou smear has become widespread, the incidence of invasive

cervical cancer has dramatically decreased. At the same time, the detection of cervical dysplasia has significantly increased. Diagnosis, management and follow up of pre invasive cervical lesions are now a major public health challenge. Pap smear test is a major screening test for early diagnosis and treatment of cervical cancer. Inflammation on pap smear is considered a relatively benign finding. However, due to the low sensitivity and high false negative rate (As high as 20%) of pap smear, there is a possibility that an inflammatory pap smear may miss cervical pre malignant changes and in rare cases malignant changes as well. Since the incidents of inflammation on pap smear is very high (14-19%), it may not be possible to subject all patients with inflammation to colposcopy or HPV DNA testing.[9] Keeping this view in mind, this study was designed to evaluate whether persistent inflammatory changes on pap smear could be the first indication of pre malignant changes in the cervix and whether further evaluation by colposcopy would help to triage these women.

In the present study a total of 64 women underwent pap test during the study period for gynecological problems like vaginal discharge, post coital bleeding, intermenstrual bleeding and leucorrhea. Of them 14 (21.9%) were reported as having inflammatory cellular changes. Anti-inflammatory treatment given to these patients cured most of them living 6 (9.34%) cases with a repeat report of inflammation on pap smear which also compares well with the study of Bhutia et al.[14] Similar results were reported by Secken et al.[9] But the prevalence was lower than that reported by Sandmire et al.[15] The prevalence of inflammatory pap smear in various Indian studies is reported to vary between 70% and 80.5%.[16] However, in a recent study, the reported prevalence was lower (24.3%) is quite consistent with the findings of the present study.

Among the unhealthy, persistent inflammatory pap smear cases, 33 (51.6%) were colposcopically positive for CIN and biopsy material histologically, exhibited abnormal cytology in 12 (36.3%) cases (CIN-1 16.6%, CIN-2 66.7% and invasive carcinoma 16.6%) which accounts for 18.1% of the 64 women with persistent pap smear included in the study. In another study, out of the 30 women with persistent inflammatory pap smear 16 (53.3%) women had abnormal colposcopic findings and CIN was found in 5 of these women meaning 16.3% women with persistent inflammatory pap smear were harboring CIN. Various studies have found the possibility of CIN with a report of persistent inflammatory smear to range from 18-35%.[9]

The mean age of the women with unhealthy cervix, persistent inflammatory pap smear was 32.6±7.2 years which is fairly comparable with the findings of other study. Comparison of age at marriage, age at first child birth and parity between patients with CIN (Including invasive disease) and without CIN revealed that the former group married and experienced child birth significantly earlier than the latter group ($p=0.001$ and $p<0.001$ respectively). The average parity was also significantly higher in the CIN group than that in women without CIN. Bhutia and colleagues reported that mean age at marriage was 18.9±2.6 years among women with persistent inflammatory smear while that with the women with CIN was 16.8±2 years ($p=0.05$).[14] The mean parity was also higher in the former group ($p>0.05$) thus favoring the findings of the present study.

According to the various studies, ASCUS (Atypical squamous or glandular cells of undetermined significance) on pap smear has a 10-20% chance of harboring CIN.[17] This is the reason why we triage women with ASCUS on pap smear with either repeat cytology, HPV DNA testing or colposcopy. Our study has shown a sizable proportion of women (About 20%) with persistent inflammation on pap smear could be harboring CIN. Moreover, the incidence of CIN and invasive carcinoma in women with persistent inflammatory pap smear over just two weeks was found increased to 20.6% and 0.7% respectively, in a study by Dasari et al.[5] Hence, by waiting for a longer period of time before repeating the pap smear may lead to a delay in diagnosis of CIN in a high percentage of cases.[5]

Chronic inflammation, either specific or non-specific, has been shown to be associated with malignancy and was thought to be one of the factors responsible for carcinogenesis. Persistent inflammation leads to increased cellular turnover, specially in the epithelium, and provides a selection pressure that result in the emergence of cells that are at a high risk for malignant transformation.[18]

Hence, all women with persistent inflammation on pap smear should be subjected to further evaluation. One must not see a report of inflammation on pap smear in isolation and ignore it as being absolutely insignificant. Following treatment with antibiotics, a repeat pap smear is needed in 2-4 weeks apart and if it persists in any patient she must be evaluated further by colposcopy.

Limitations

The limitations of the study were as follows:
Small sample size of the study population, the study population was selected from one selected hospital in Chittagong city, so that the results of the study may not be reflect the exact picture of the country. It was conducted in a tertiary care hospital which may not represent primary or secondary center. A large-scale study needs to be conducted to reach a definitive conclusion.

Conclusion

Cervical lesion is the commonest problems among females worldwide. In many developed and developing countries a declined in the incidents and mortality due to cervical cancer has been observed due to screening. On the basis of the findings of the study it can be concluded that patients with persistent inflammatory pap smear can harbor a high proportion CIN and sometimes even early stage of invasive carcinoma. Pap smear and colposcopy in screening for CIN and cervical cancer is very effective tool for early detection of cervical cancer.

Recommendation

Every precancerous cervical lesion should be advised to evaluation of disease by colposcopy, which will reduce the fatal outcome of patients. Every malignant lesion should be evaluated early and staging should be done to assess curative or palliative operation. Every medical person should take prompt and necessary action for managing cervical cancer which will reduce the morbidity and mortality. A health care policy should be formulated with wide range publicity for developing awareness of precancerous cervical lesion patients for early detection and management.

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Contribution of Authors

NF- Conception, design, acquisition of data, drafting and final approval.
MK-Acquisition of data, interpretation of data, data analysis, critical revision and final approval.
AAM-Acquisition of data, interpretation of data, data analysis, critical revision and final approval.
TI-Acquisition of data, interpretation of data, data analysis, critical revision and final approval.
AAB-Acquisition of data, interpretation of data, data analysis, critical revision and final approval.

Disclosure

All the authors declared no competing interests.

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