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Cytology screening for cervical cancer by conventional Pap smear: Experience at private hospital and diagnostic centre catering to sub urban population

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Abstract
Background: Study of cervical cytology smears is the most popular effective screening tool for picking up precancerous lesions in asymptomatic women. Wide variability exists in the incidence of different cervical lesions contributed by complex geographic, socioeconomic, religious and cultural factors. The current study aimed to explore the spectrum of cervical cytology lesions and its presentation.
Material and methods: The study was done at our private hospital and diagnostic centre catering to suburban and rural population. Institutional ethical committee clearance was obtained. Cases with colposcopicaly visible masses and those with inadequate clinical details were excluded from the study. A structured questionnaire was administered to consenting patients, to access awareness about cervical cancer and to obtain crucial data pertaining to their clinical history. 600 cases of cervical and vaginal vault smears collected over a period of 10 months from January 2019 to October 2019 were rescreened and reported as per The Bethesda System for reporting cervical cytology. The spectrum of cytological diagnosis observed was compared with that of similar studies. Also the most common clinical presentation was analysed.
Results: We received samples from a wide age group of married women ranging from 16 to 83 years. Most of the participants (82.6%) undertook the test as part of Routine screening, under evaluation for other gynaecological issues. 17% of participants underwent the test as part of general health check-up. Only 3.67% of participants were aware of Pap smear being a screening test for cervical cancer. Menstrual cycle abnormalities was the most common gynaecological complaint among the participants, followed by cervical discharge. Of the 600 women screened, 27.86% were reported to have NILM with reactive changes, 14.87% showed evidence of a cervical microbial infection with bacterial vaginitis, trichomoniasis or candidiasis while 15.56% had epithelial cell/glandular abnormalities. Among the latter, premalignant lesions constituted 3.43% and malignant lesions constituted 0.34%. Infections were more common in younger age group.
Conclusion: Multiple nationwide coordinated population studies are hence beneficial to understand local trends in the spectrum of cervical lesions and their clinical presentation. This becomes ever relevant in a largely conservative society with limited reproductive health awareness and resource poor setting where conventional cytology smears continue to save thousands of lives.

Keywords: Cervical cytology, Pap smear, cervical malignancy, opportunistic screening, Bethesda system for reporting cervical cytology

Introduction
Cytological study of cervical smears has been historically one of the greatest contributions of medicine for effective cancer screening in asymptomatic patients [1]. The benefits have time and again been proven by various cross sectional studies and large scale clinical trials performed ever since its introduction as a mass screening tool as part of public health care programmes mostly implemented in developed countries [2]. Although it comes with an inherent margin of significant false negative rates, the sheer number of precursor lesions of cervical cancer picked up by a test so convenient and affordable, testifies to its popularity [4].
It is however unfortunate that there exists a glaring difference in the incidence of cervical cancer among resource poor developing countries and among developed countries [5, 6]. Worldwide, studies have shown variability in the baseline spectrum of cervical lesions as picked up from the study of Pap smear cytology [3].

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Numerous factors have been quoted as reason for this variation in local cancer incidence, resonating with the geographical, socio-economical, religious, cultural factors, sexual profile, health care seeking behaviour, prevalent strains of oncogenic HPV infections and inherent genetic susceptibility [7, 8, 9, 10, 11, 12]. India shares a major burden of deaths by cervical cancer. The reported incidence of cervical cancer adjusted for age from different states in India varies from 6 to 29% of all cancers in women [13]. Introduction of a standardised reporting system by The Bethesda System (TBS) for Reporting Cervical Cytology has had profound impact on sensitivity and specificity of pap smear for detecting Lesions like LSIL and HSIL [14]. Still, the factor of observer variability persists to a certain extent [1, 4, 15, 16, 17].

Our study tries to explore the spectrum of cervical cytological diagnosis in the local population. We also analysed the health care seeking behaviour and the most common clinical presentation of patients undergoing the Pap smear procedure. This is even more pertinent as awareness on Reproductive health remains unfortunately inadequate in a largely conservative society which considers discussion of gynaecological issues as taboo [16].

Material and Methods

The study was conducted at a private hospital and diagnostic centre for a period of of 10 months from January 2019 to October 2019, where all cervical and vaginal vault smears received were stained with Rapid Pap stain and carefully screened by trained and experienced cyto-pathologists and the spectrum of cytological diagnosis were reported as per The Bethesda system for reporting cervical cytology. We have a strict protocol at place in our institute for reducing the observer variability. Lower false negative and false positive error rates are achieved by rescreening 20% of all cases reported negative and targeted rescreening of all positive cases.

Cases with history of evident mass on colposcopic examination and those with inadequate data were excluded from the study. In addition to clinical data collected from requisition forms, patient was also administered with a structured questionnaire to collect relevant information pertaining to medical history and presenting complaints. The answers were analysed to obtain an insight into level of health awareness and health care seeking behaviour for reproductive tract diseases. All 600 samples collected were rescreened by a different pathologist of equal standing and experience in reporting cervical cytology smears. The percentage of cases falling under different diagnostic categories as reported by The Bethesda System for Reporting Cervical Cytology were compared with those from similar studies in the country. Sachan The most frequent clinical presentation of different lesions were analysed.

Results

In our study, we received 600 samples from age group ranging from 18-83 years, all from married women. In 496(82.6%) women the test was requested as part of routine screening, under evaluation for other gynaecological issues and in 102 (17.0%) participants, the test was performed as part of general health check-up. Only 22 cases (3.67%) of participants were aware of the purpose of the screening test performed. Menstrual cycle abnormality (irregular cycles/ increased bleeding) was the most common gynaecological complaint among the participants constituting 31.5%, followed by vaginal discharge or itching (25.5%) and severe lower back ache unrelated to menstrual cycle (22.5%). (Refer Table 1. Symptom-wise break up of most common complaint or clinical presentation).

2.5% of samples were inadequate/Unsatisfactory for opinion. Of the remaining 585 samples, 15.56% showed epithelial/glandular cell abnormality while total of 95.53% were Negative for intraepithelial lesion or malignancy (NILM). Of the non-malignant lesions, 27.86% showed reactive changes associated with inflammation, 14.87% showed evidence of a cervical infection consistent with bacterial vaginitis, trichomoniasis or candidiasis and 12.82% were reported as atrophic smears. Evidence of infection was most common in the age group of 21-30 years followed by 31-40 years. The frequencies of ASC-US (Atypical squamous cells of undetermined significance), ASC-H (Atypical squamous cells- cannot exclude HSIL), LSIL (Low Grade Squamous Intraepithelial Lesion), HSIL (High Grade Squamous Intraepithelial Lesion) and Carcinoma of cervix was 1.54%, 0.17%, 12.82%, 0.68% and 0.34% respectively. (Refer Table 2 Distribution of cytological smears with most common age group at diagnosis.

Table 1: Symptom wise distribution of patients

Symptoms	Number of patients	Percentage (%)
Menstrual irregularities	189	31.5
Vaginal discharge	153	25.5
Pain abdomen	97	16.17
Post menopausal bleeding	30	5.0
Post coital bleeding	5	0.83
Increased frequency of urination	30	5.0
Feeling of Mass through vagina	59	9.83
Severe low back ache unrelated to Menstruating days	135	22.5
Asymptomatic	155	25.5

Table 2: Distribution of cytological smears with most common age group at diagnosis.

Cytological diagnosis	No of cases	Percentage of Cases (%)	Most common age group
Inadequate smears	15	2.5	21-30
Nonmalignant	553	95.53	31-40
Negative for intra epithelial lesion or malignancy	228	38.97	31-40
-Negative for intra epithelial lesion or malignancy with inflammation	163	27.86	31-40
-Negative for intra epithelial lesion or malignancy with microbial infection	87	14.87	21-30
-Atrophic smears	75	12.82	61-70

Epithelial cell abnormalities	91	15.56		
ASCUS	9	1.54	51-60	
ASC-H	1	0.17	51-60	
LSIL	75	12.82	31-40	
HSIL	4	0.68	41-50	
SCC	2	0.34	51-60	
Total	600			

* ASC-US-Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells- cannot exclude HSIL; HSIL: High Grade Squamous Intraepithelial Lesion; LSIL: Low Grade Squamous Intraepithelial Lesion; SCC - Squamous cell carcinoma.

Discussion

Statistics from prominent cancer registries have shown high cervical cancer mortality in India with cervical cancer being the commonest cancer in Indian women [17]. Much saddening is that these deaths are largely preventable given the long latency of the precancerous lesions and the moderate sensitivity of simple Pap smear cytology in picking up of these early lesions. Proactive National health awareness programmes with large scale community screening are proven strategies in reducing cervical cancer mortality [2]. Shankaranarayanan *et al.* in their review article suggest that middle-income developing countries should essentially target high risk groups and follow a realistic approach using highly sensitive tests. Policy makers could learn from lessons from the past failures and experiences of different countries' cytology screening programmes.

Awareness about cervical health was indirectly accessed using questions directed at their understanding of nature of test procedure and their reason for undergoing it. From our study it was evident that all patients underwent the Pap smear testing as part of workup of gynaecological complaints at the advice of a gynaecologist or as part of either general checkup. We conclude that cytology referral by self-request i.e. the number of patients requesting the clinician themselves for a cervical cancer screening test is non-existent. We hence are also of a strong opinion like many other health care providers that at least an opportunistic screening approach should be followed by the vast majority of private medical colleges and private hospitals, until an integrated national policy for mass screening of general population is implemented by the Government of India [18].

The percentage of inadequate smears was comparable to most similar studies [3, 18, 19]. Infections are common in younger age group while precancerous lesions are common in the age group of 31-40 and carcinomas are common in older age groups similar to various other studies [18, 20]. However, the percentage distribution of various cytological lesions from our study showed significant variation when compared with those of similar studies conducted from various parts of the country and the world. (Refer Table 3: Comparison of percentage of distribution of cytological cases with similar studies). This is all the more pertinent since nation-wise, there exists wide variation in the spectrum of different categories reported from different states and within districts of these states [13, 17]. Coordinated opportunistic screening of smaller cohorts should be undertaken throughout the country by the 542 odd private medical colleges in India and integrated with those of repositories of crucial data like the National Centre for Disease Informatics and Research (NCDIR) which is a permanent unit of the Indian Council of Medical Research. NCDIR corroborates crucial data from cancer registries located in medical colleges/institutions and hospitals throughout India [20]. This approach will help ascertain the prevalence of precancerous lesions in a geographically and ethnically pleomorphic country like India and help plan rolling out to large scale population screening programmes. The main limitation in our study was the socioeconomic spectrum of patients attending our private hospital and diagnostic centre may not be representative of the true population status as people belonging to the lower strata prefer government sponsored services. It is this population that has lower reproductive health awareness and in need of proactive screening by Pap smear as pointed out by several studies [6]. The burden of epithelial precursor lesions picked up by pap smear cytology can hence be larger than the findings in our study. Another limitation is correlation with findings from colposcopic visual inspection by acetic acid and HPV DNA testing results. However given the lower specificity and higher cost of setting up of facilities for HPV DNA testing and visual examination by acetic acid, competently conducted cytological testing by Pap smear should be considered as gold standard and can itself significantly help reduce cancer burden [3]. The wide range of variation in sensitivity has to be addressed by setting up good sample collection practices, processing protocols and by proper training of staff involved.

Table 3: Comparison of percentage of distribution of cytological cases with similar studies.

Categories	Our study	Sachan et al.	Kulkarni et al.	Ghosh et al.	Syrjanen et al.
Inadequate	2.5	6.42	2.57	2.3	0-2
NILM	94.53	91.50		99.8	93.6-95.7
Normal	38.97	48.84	11.73		
Nilm with inflam	27.86	42.66	73.90	15.3	
NILM with Infec	14.87		1.76	12.4	
Atrophic	12.82		1.66	8.3	
Epithelial cell abnormality	5.47	8.48	12.61	0.2	4.3-5.5
ASCUS	1.54	2.90		0.1	1.5-3.8
ASC-H	0.17				
LSIL	2.74	5.09	7.62		0.9-1.2
HSIL	0.68	0.48	4.39	0.1	0.4-1.0
SCC	0.34	0	0.59		0.1-0.3
Non malignant to malignant ratio	17.28:1	10.79:1	6:1	499:1	

Conclusion

Cervical cancer awareness in Indians is abysmal in spite of the nation's alarming cervical cancer burden. The Bethesda system of reporting cervical cytology has vastly reduced the inconsistencies in reporting of cervical cytology smears. Data from various centres in the country show that there still exists wide variation in percentage wise reporting of different cytological lesions on Pap smear. There exists no doubt that the institutions should ensure their testing procedures are conducted efficiently. Also, the nature of variation and the contributing factors behind these variations needs to be accessed, by numerous coordinated population based studies in various parts of the country if we are to rely on national screening programmes based solely on conventional cytology smears, given that additional tests like HPV DNA testing and VIA would be burdensome.

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