Cytopathological study of Cervical Smear: A Hospital Based Retrospective Study

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ABSTRACT

The present study aimed to analyze the Pap smear for cytopathological evaluation in a hospital based community at National Institute of Unani Medicine (NIUM), Bangalore.

A retrospective study was conducted at pathology laboratory, NIUM from June 2010 and June 2012. A total of 700 married women were included aged 18-70 years with abnormal vaginal discharge and who had come for cervical cancer screening. The Pap smears were obtained by using conventional technique and were evaluated using The Bethesda system 2001. The data was analyzed statistically.

The overall Pap smears analysis showed 18.2%, 1.2%, 67.1% and 1.8% of normal, inadequate, inflammatory and low grade squamous intraepithelial lesions (LSIL) respectively. Of 67.1% of inflammatory smear, 8.2%, 35.7% and 23.1% were mild, moderate and severe inflammatory smear respectively. The inflammatory smears in Muslims and Hindus were found in 68% and 64% respectively. The low-grade squamous intraepithelial lesion was observed in 1.4% and 3% among Muslims and Non-Muslims respectively. The mean age was 34.69±9.15 years and most of the women were in reproductive age group.

In this study, the epithelial cell abnormality (LSIL) was found to be low in Muslims than Non-Muslims in Cytopathological evaluation of cervical smear. Hence, this study proves that in Muslim community the prevalence of cervical dysplasia is less. It is also recommended that reporting should be done by using The Bethesda System, as it improves the reproducibility and plays a key role in diagnosis of various intraepithelial lesions at an early stage.

Key words: Cervical cancer, Pap smear, Bethesda System, LSIL, Epithelial cell abnormality

INTRODUCTION

Cancer has become an important contributor to the global burden of diseases and one of the most dreaded non-communicable diseases. It brings incredible, physical and psychological suffering, social distress, hardship to patients and their relatives. All over the world efforts are on to prevent and control this disease. Information on epidemiology of cancer viz., prevalence, incidence, pattern and high risk factors are essential to plan, implement, and to evaluate control of cancer. However, these are not available for most of the less developed nations of the world [1]. According to the survey, in the age group of 30-69 years, the three most common fatal cancers, were oral (23%), stomach (13%), and lung (11%) in men, and cervical (17%), stomach(14%) and breast (10%) in women [2]. Cervical and breast cancer are common cancers among women in most of the developing countries of the world. However, in the developed countries breast cancer is the leading cancer in women. Recent reports of registries from India has shown that in most of the urban registries breast cancer incidence has overtaken cervical cancer incidence [1].

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In 1980, cervical carcinoma was the second most frequent cancer in women throughout the world, accounting for 15% of the malignancies. Because of widespread differences in the availability of screening programs and the prevalence of risk factors, there is a marked variation in the relative frequency of cervical cancer in developing countries. The highest incidence rates have been reported from sub-Saharan Africa, Central and South America, Southeast Asia and Brazil. The lowest reported incidence rates are from the Middle East, where the incidence is particularly low among Muslims and Jews, as compared to other religious groups [3]. In India, cervical cancer is the second most common cancer among women. In 2007, the estimated number of new cases according to national cancer registry of India was 90,708 with 5-year survival rate of about 48%. It is estimated that in India 126,000 new cases occur each year [4]. Fortunately, the natural history of cervical cancer is such that it is possible to detect it early during a preinvasive stage by screening and early intervention, thereby preventing progression into a life threatening illness [5]. Various methods of screening cervical cancer include Papanicolaou smear, visual inspection method using acetic acid (VIA) and Lugols iodine (VILI) and HPV DNA testing. However, it is well established in literature and clinical practice that the best method for early detection of precancerous lesions of cervix is cytological examination by Pap smear [4]. In 1941, Papanicaloau described cervical mass screening for sexually active women for early detection of cervical cancer [3]. It now ranks as the sixth cause of cervical mortality in developed countries [6] because of remarkable improvement that has been attributed largely to cytological screening for cervical cancer by Papanicolaou method The easy accessibility of the cervix and the propensity of the cancer cells to exfoliate from its surface have enabled us to study the process of malignant transformation in the cervix in very early stage [7]. Despite this fact, 75% of women in India present to the health facility in advanced stages of the disease hence screening for cancer of the cervix remains a neglected health care issue [4].

Numerous studies have been carried out in various countries to analyze cervical cancer in community and hospital based study [1, 8, 9 10, 11]. In India, Cytopathological study of cervical smear in Muslim community has been carried out in Assam, Kashmir [4], Rajkot [7], Mumbai [5], Udupi district (Karnataka) [12]. However, till date none of the studies in west Bangalore (Karnataka, India) has analyzed the Pap smear for Cytopathological study in the early detection of carcinoma of the cervix, and to address the need for cancer screening programs in order to properly estimate the magnitude of Cervical Cancer. Hence, the present study was conducted with the aim to analyze the Pap smear for Cytopathological evaluation in a Hospital based study.

MATERIALS AND METHOD

Study design

The present hospital based retrospective study of Pap smears was conducted between June 2010 and June 2012 in the National Institute of Unani Medicine (NIUM). This institute is affiliated to Rajiv Gandhi University of Health Sciences, a Post graduate research institute of Unani Medicine, Ministry of Health and Family Welfare, Govt of India, situated in Bangalore, Karnataka, India. The results of Pap smear of 700 participants were collected from the cytology section which was reported by cytopathologist (pathology laboratory) of this institute.

Participants: Married women aged 17-70 years with relevant gynaecological complaints (abnormal vaginal discharge, menstrual abnormalities, low backache, infertility, unhealthy cervix, postmenopausal bleeding, postcoital bleeding) or presented for routine screening for cervical cancer in cervical cancer awareness month (January) were included in the study. None of the patients However, participants having vaginal bleeding other than postcoital or postmenopausal, inadequate sample, pregnant woman, recent vaginal delivery and patients with frank cervical cancer was excluded. The details of participants were reviewed and information regarding demographic data, relevant gynaecological complaints was assessed. The relevant clinical data were collected by gynaecologist including age of patients, age of marriage, menstrual history, and parity and presenting complaints. Routinely in this institute gynaecologist ensured that before taking the cervical Pap smears, the patient was not menstruating, had not douched or used tampons or vaginal medication for the preceding 24 hours. In all cases, the cervical smear was taken from the endocervix and the squamous-columnar junction with an Ayers spatula, after insertion of a bivalve vaginal speculum. These samples were smeared on glass slides, one fixed with 100% methanol and other dry smear were submitted to the pathology department for reporting. All cervical smears after fixing were stained by Pap stain, H&E and Giemsa stain. After staining the samples were examined and reported by a qualified cytopathologist under a light microscope.

Cytologic tests: The entire smear was classified according to the modified Bethesda system 2001 [9, 13]. In this classification, a low-grade squamous intra-epthelial lesion incorporates mild dysplasia while a high-grade squamous

TABLE 1: Age distribution and symptoms of the participants.

Age (Y)	Participants (n=700)	Muslim (n=535)	Non-Muslim (n=165)
<20	5(0.7)	5	0
20-29	195(27.8)	157	38
30-39	309(44.1)	229	80
40-49	138(19.7)	104	34
50-59	36(5.1)	28	8
>60	17(2.4)	12	5
Total	**700(100)**	**535**	**165**
Symptoms	Participants (n=700)		
Discharge	438 (62.5)		
Menstrual abnormalities	38(5.4)		
Low back ache	5(0.7)		
Infertility	24(3.4)		
Unhealthy cervix	10(1.4)		
Postmenopausal bleeding	20(2.8)		
Screening	105(15)		
DUB	16(2.2)		
Others	44(6.2)		
Total	**700(100)**		

Data presented: No (%)

intraepithelial lesion includes the moderate, severe and carcinoma-in-situ categories [11]. Specimen adequacy was determined based on the presence of endocervical cells, as well as adequate numbers of squamous epithelial cells (more than 10% of the slides containing squamous cells) [2]. According to Coste el al., Pap smear method had 72% sensitivity and 94%specificity and suitable for population based screening programme [14]. Pap smear testing also has strengths, such as wide acceptance, meeting most of the criteria for a good screening test in settings with adequate resources, obtaining a permanent record of the test in the form of a slide, and having a high specificity of 60-95% [9].

Statistical analysis: The Statistical software Graph Pad Instat version 3.00 for window (Graph Pad Software, San Diego, Calif, USA) was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Simple percentage of the lesions were calculated and compared with each other. Frequency distributions and descriptive statistics were calculated. Data were reported as number (percentage) or mean values standard deviation.

RESULTS

During the study period, data of 700 pap smears was analyzed. The mean age (SD) was 34.699.15 years and most of the women were in reproductive age group. Majority of the participants (44.1%, n=309/700) were between the age group 30-39 years and only 5(0.7%) were less than 20 year of age (Table 1). In this study, total no of Muslims and non-Muslims were 535 (76.5%) and 165 (23.5%). The symptoms of participants are summarized in Table 1. According to classification of smears by Bethesda system the Cytopathological findings of smear was normal, inflammatory, postmenopausal, bacterial vaginosis, candidiasis, and epithelial cell abnormality in 128(18.2%), 470(67.1%), 30(4.2%), 38(5.4%), 7(1%) and 13(1.8%) respectively (Figure 1). The commonest lesion was inflammatory followed by normal smears (Table 2). The cytopathological findings in Muslim and non-Muslim are summarized in Table 3.

DISCUSSION

Worldwide in women, cervical cancer is an important cause of morbidity and mortality more so in developing countries.

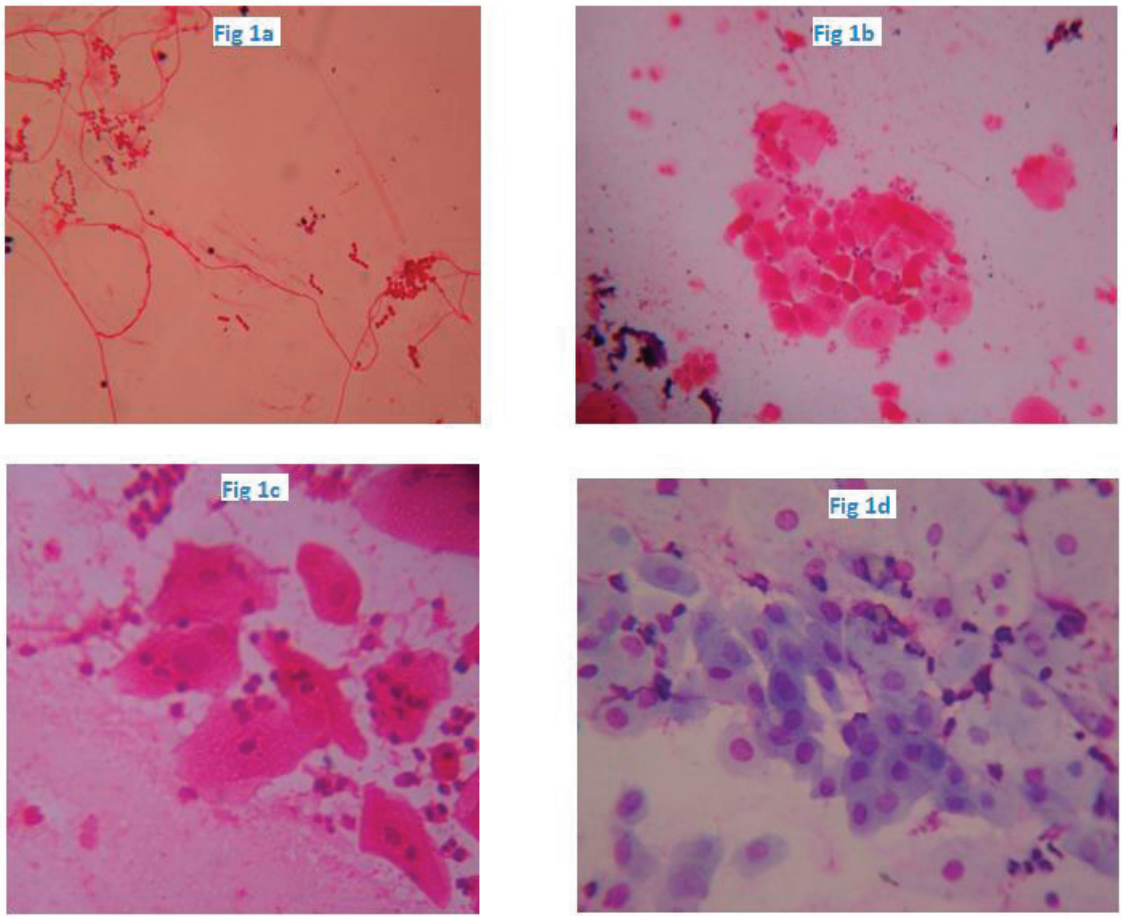

Figure 1: Cervical smear (conventional Pap): 1a: 40 x HPE showing fungal hypae; 1b: 40 x HPE showing post menupausal atrophic smear; 1c: 40 x HPE showing inflammatory smear; 1d: 40 x HPE showing dysplastic cell (LSIL).

Cervical cancer is an ideal gynaecological malignancy as its meets both test and disease criteria for screening. This disease has a long latent phase during which it helps us to detect the premalignant lesions which proceed to the invasive disease. Cervical cancer screening can be done with various tests such as conventional exfoliative cervicovaginal cytology, liquid based cytology, automated cervical screening, HPV tests, laser induced fluorescence, visual inspection by using Lugols iodine/ acetic acid, etc [4]. Cytological examination of Pap smear for early detection of precancerous lesions of cervical cancer is one of the best method and this has been well established in the literature as well as in routine clinical practice [3]. Papanicaloaus technique is regarded as the gold standard test as it satisfies the test criteria for a screening. It is a simple, easy to perform, cost effective, safe, valid procedure especially in hospital or population based screening programme and thus it has altered the course of disease in cervical cancer patients [4]. Conventional cytology by Pap technique is used in this hospital as maximum number of participants belongs to low socioeconomic status.

In the present study, Pap smears revealed Epithelial cell abnormality (LSIL; n=13(1.8%)),and light microscopy showed the presence of atypical cells which were seen in sheets and at places scattered against an inflammatory background. Nuclear abnormalities were seen in these cells which were three times the nuclei of normal cell,resulting in an increased nuclear/cytoplasmic ratio. The nucleolus was not seen and nuclear membrane abnormality was seen in few cells with irregular chromatin condensation. It is important to note that cells showing perinuclear halos in the absence of nuclear abnormalities did not qualify for the diagnosis of LSIL.

TABLE 2: Distribution of participants according to Cytopathological findings as per Bethesda system of classification.

Findings	No of patients (n=700)
Inadequate	**9(1.2)**
Others (Normal)	**128(18.2)**
Reactive Changes	
Mild	58(8.2)
Moderate	250(35.7)
Severe	162(23.1)
Atrophy	30(4.2)
Radiation	0
IUC	0
Others	05(0.7)
Benign Cellular changes	
Trichomonal	0
Bacterial vaginosis	38(5.4)
Candida	7(1)
Actinomycosis	0
HSV	0
Others	0
Epithelial cell abnormality	
SCC	0
ASCUS	0
LSIL	0
HSIL	13(1.8)
CIS0	
Glandular cell abnormality	**0**

Data Presented: No(%)

Symptoms: In the present study, symptoms suggestive of reproductive tract infections were reported by the females, which included abnormal vaginal discharge (n=438/700, 62.5%). This finding is in agreement with the previous study. Another study showed that the commonest clinical signs/ symptoms seen among the 102 patients with neoplastic gynaecological lesions were abnormal vaginal discharge and postmenopausal bleeding (93/102; (91.2% and 62/102; 60.7%) [10]. Reproductive tract infection as a risk factor for cervical cancer has been evaluated by several studies. However, some studies have noted that genital tract infection is a poor predictor, as a risk factor for cervical cancer. Contradictory, a study conducted in India has reported positive association and found that there was equivalent increase in the proportion of women with cervical dysplasia, who had the symptoms of reproductive tract infections. Their study concluded reproductive tract infection is exacerbated by poor genital hygiene which has a role in development of cervical dysplasia and cervical cancer. Similarly, another Indian study has found infections of reproductive tract as one of the risk factor for cervical cancer [4].

In this study, 76.5% (n=535/700) were Muslims and 23.5% (n=165/700) were Hindu women who reported for Pap test. This finding is in accordance with study conducted by Aras et al. (Muslims 76.3%. Hindus 22.6%) [5]. The predominant population attending this hospital belongs to Muslim community.

In the present study, cytological analysis showed 128 (18.2%) normal smear, 470 (67.1%) inflammatory smear, and 13 (1.8 %) epithelial cell abnormality. In the present study, the inflammatory changes were seen in 67.1%, whereas study conducted in Kuwaitis showed inflammatory changes in 42.1% (n= 17,593/ 41,748) [8].

In this study, the prevalence of cervical dysplasia constitutes 1.8% which correlates with the other studies. In an ICMR

TABLE 3: Distribution of Cytopathological findings among non-Muslim and Muslim.

Age (Y)	NA		N		Mi		Mo		S		BV		Can		R		LSIL		Atrophy		Others		Total	
	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	N M	M	NM	M
<20	0	0	0	1	0	2	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	5
20-29	0	3	5	26	3	13	17	57	10	41	3	13	0	3	0	1	0	0	0	0	0	0	38	157
30-39	1	2	15	50	4	24	30	92	22	47	5	9	0	2	1	0	2	2	0	0	0	1	80	229
40-49	0	2	9	19	2	6	6	37	10	26	3	5	1	1	0	1	2	4	1	3	0	0	34	104
50-59	0	0	1	2	1	3	0	9	1	3	0	0	0	0	0	0	0	1	5	10	0	0	8	28
>60	0	1	0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	1	3	8	0	0	5	12
Total	1	8	30	99	10	48	53	197	43	119	11	27	1	6	2	2	5	8	9	21	0	1	165	535

Data Presented: Number; NA: Not Adequate; Mi: Mild; Mo: Moderate; S: Severe; BV: Bacterial Vaginosis; Can: Candidiasis; N: Normal; R: Reactive; LSIL: Low grade Squamous Intraepithelial Lesion; NM: Non- Muslims; M: Muslim

study conducted at Delhi, prevalence of dysplasia and malignancy was very low which constituted 2.3 % and 0.2 % respectively [15] A study conducted in rural population of Wardha district revealed similar results[16]. The prevalence of cervical dysplasia in Muslim population was 1.4% in the present study which is slightly higher when compared to study which was done in Pakistan. According to one more study conducted at Bangalore there has been decline in the incidence of rate of cervical cancer in Bangalore. The decline of cancer of cervix in developing countries like Bangalore is due to increase in age at marriage due to changing socio economic environment [17]. In a study, initiated at Institute of Cytology and Preventive Oncology (ICPO), New Delhi, on uterine cervical dysplasia showed an interesting finding that all malignant lesions were found in Muslim women [18] and the researchers justified it may be due to the fact, that it was predominantly Muslim community (76.3 per cent of study population). However, also similar studies were conducted Pune city and greater Bombay with predominant Hindu females revealed higher incidence of cervical cancer than Muslim females [19]. One more study conducted at Pune City found the incidence of cervical cancer in Hindu and Muslim females was 22.7 per cent and 4.6 per cent respectively [5]. India has the highest prevalence of cervical cancer in the world and also has a substantial Muslim population; however, low prevalence of cancer cervix has also been reported among Muslims (13.4%). The probable reason for absence of cervical dysplasia and cancer could be the religious and socio-cultural practices prevalent among the Muslim society that include compulsory male religious circumcision and marked absence of promiscuity. Significant evidence from pooled data of case control studies on cervical cancer showed that male circumcision reduces the risk of HPV infection among men cervical cancer among women with high risk sexual partners. This is further supported by other studies [4].

In this cytological study, Pap smear results showed a low rate of atypical cervical epithelial cell abnormalities among the study population. However, these results should be regarded cautiously due to the low sensitivity of Pap smear testing. The researchers did not have the opportunity to evaluate the results with other more sensitive tests like AAT (acetic acid test) and HPV identification. In this study the majority of Pap smears were evaluated as inflammatory smear (67.1%),and 13.8 (1.8 %) epithelial cell abnormalities. Similar results were obtained from other studies done both in hospital or primary health care settings: 50.6% infections; 49.8% infection. These results show that vaginal infections are important and may be a public health problem that should receive more attention. The low frequency of atypical epithelial cell abnormalities in this study could be due to a low-risk Muslim population [9].

The peak age for epithelial cell abnormality in this study was between the age group of 30 to 49 years. This is in consistent with study done in Pakistan [11] as patients attending this hospital are not educated and do not have any awareness of the cancer. This is not in accordance with the results of a North American study reporting peak age-specific dysplastic cytology in the 23 to 34 year age group [20]. This difference may be due predominant Muslim community and they have lower prevalence of risk factors, such as multiple sexual partners, smoking and the use of oral contraceptives. All the 13 patients who had epithelial cell abnormality were subjected to colposcopic biopsy followed by HPE. However, they were lost in follow up as no surgery or biopsy is under taken in this institution hence they were referred to others places following which the patients were lost. Loss of follow up is common in most developing countries and is clearly the same problem we faced in our study as well.

The strength of the study was it is first kind of its study in west Bangalore analyzing cytopathological finding of Pap smear in specific hospital based community and bringing awareness in the population of the hospital. However, the limitations study were because of retrospective study, follow up of the patients was not possible, the results were not evaluated with other more sensitive tests like AAT (acetic acid test),colposcopic biopsy and HPV identification. Further, prospective study to find the prevalence of cervical cancer, correlation with risk factors, using more sensitive tests, HPV identification are recommended.

For the future, the challenge for us is to increase awareness regarding cervical cancer among the patients. Education would play a major role in success of detecting early precursor lesion in the female patient. Lecture and tutorials utilizing audiovisuals facilities in hospital waiting areas would be helpful. The reporting of cytological smears should follow unified reporting system and unified methods of follow-up of normal or abnormal results. The reporting should be done by qualified cytopathologist and all abnormal smears should be subjected to Colposcopic biopsy.

CONCLUSION

Suitable methods for early detection of cervical cancer like Pap smear testing should be organized on a wider scale for controlling this disease. Pap smear is a simple, cheap, safe and practical diagnostic tool for early detection of cervical cancer in high risk group population and therefore should be established as routine screening procedure. It is a valuable tool for investigation as a screening procedure as a diagnostic procedure in symptomatic women. It also has an important role in diagnosis of inflammatory lesions including the identification of causative organism, atrophic changes, changes of radiation therapy and some rare tumors. In this study, the epithelial cell abnormality was found to be low in Muslims than non-Muslims in Cytopathological evaluation.

It is recommended that reporting should be done by The Bethesda System as it improves the reproducibility and helps in identification of ASCUS and AGUS lesions and plays a key role to diagnose various intraepithelial lesions and invasive lesions at an early stage and manage them properly.

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CONFLICT OF INTEREST: None

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