RESEARCH ARTICLE

Socio-demographic and Clinical Characteristic of Women Availing Pap Smear Services in Samtse District, Bhutan

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Abstract

Background: The case burden of cervical cancer has been increasing globally especially in developing countries without proper health system. Cervical cancer can be eliminated with timely vaccination and screening program as it usually takes years for pre-malignant lesions to develop into malignant lesion. Bhutan has committed to eliminate cervical cancer. Thus, it is important to understand the factors associated with abnormal Pap test findings. **Methodology:** A retrospective study was conducted using the Pap smear data for the year 2018. It was extracted from the records maintained in the cytology unit of Samtse General Hospital. **Result:** The abnormal slide rate in this study was 2.5%. The majority of women seeking Pap smear services were women in reproductive age group and housewife by occupation. There were significant differences between age groups and marital status among normal in the Pap test results. **Conclusion:** The slide abnormality of Pap smear in Samtse District is low. The abnormality is more common among married and older women. Therefore, additional screening efforts needs to be put into this group to detect pre-malignant lesions.

Keywords: Pap smear- cervical cancer- Asia- Bhutan- HPV- human Papilloma virus- developing country

Introduction

Cervical cancer is the fourth most common cancer affecting women. In 2018, at least 0.57 million cases of cervical cancer were diagnosed globally accounting for 6.6% of all cancers among women [1] and 7.5% of total deaths from cancer among females [2]. The majority (90%) of the deaths occurred in low- and middle-income countries [3-4]. The South East Asian Region alone contributes to about 35% of the global burden of the disease [4].

Unlike other types of cancers, cervical cancer is usually preventable with vaccination. Moreover, patients tend to have high survival rate if diagnosed and treated at early stages. There are mainly two types of cervical cancer. The squamous cell carcinoma constitutes around 70% of the cases and adenocarcinoma constitutes 20% of all cervical cancer [5]. An estimated 99-100% of the cervical cancers are attributed to Human Papilloma virus (HPV) infection with, HPV 16 and HPV18 alone accounting for almost 70% of the cervical cancers [6].

Nonetheless, 90% of the infection with HPV tend to be transient and doesn't cause any dysplasia. Since the virus is transmitted through sexual route, women with multiple sexual partners, early sexual activity and multiple pregnancies are at higher risk for developing cervical cancer [7]. Cervical cancer takes around 10-20 years to develop from pre-cancerous to cancerous stage [8]. Therefore, timely screening and treatment helps in detection of this pre-cancerous lesions before it progresses to malignancy. Currently, WHO recommends three different types of screening test for cervical cancer. These include HPV testing, visual inspection with acetic acid (VIA) , conventional Papanicolaou (Pap) smear or liquid based cytology [2]. The main stay of screening for cervical cancer in most developing countries is Pap smear, although it has sensitivity of only 55.4% and specificity of 96.8% [5].

In developed countries with well-established screening and treating programs, the incidence of cervical cancer

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has decreased by almost 80% [9]. The American Cancer Society and American College of Obstetricians and Gynecologists (ACOG) guideline recommends Pap smear screening from 21 years of age regardless of sexual activity, repeated every three years thereafter. In addition, HPV testing should also be carried out along with Pap smear every five years for women in the ages of 30-65. However, annual screening is recommended for immunocompromised patients or those with history of pre-malignant or malignant lesions [6].

In Bhutan, cervical cancer is the most common cancer among women [10]. Annually, an estimated 48 cases of cervical cancer are diagnosed in Bhutan with around 32 deaths [11]. Cervical cancer accounted for 7.2% of the total 1,357 cancer cases in 2017 [12]. The age standardized incidence of cervical cancer for Bhutan is 14.4 per 100,000 and age standardized mortality rate is 10.2 per 10,000 [10].

In Bhutan, the quadrivalent HPV vaccination was first introduced in 2010 and became the first nation in the region to have implemented population based HPV vaccination [4]. Currently, HPV vaccination has been incorporated in the national immunization program and is given to all girls between ages of 9-13 years before the start of the sexual activity. Bhutan has committed for elimination of cervical cancers. The main strategy is through early detection and treatment of pre-cancerous lesion. Pap smear screening is one of the most organized and successful programs and is provided free by the government. It is carried out at all tiers of the health system ranging from basic health unit to referral hospitals. The National cancer screening manual of Bhutan recommends screening for all women in the age of 25-65 irrespective of vaccination status and repeated every three years if normal [13].

Samtse district is one of the largest districts located in the South west of Bhutan. It borders the Indian state of West Bengal. It has an estimated population of 62,590 [14]. There are two hospitals, two BHU-1 and 13 basic health units. Samtse General Hospital has a cyto-technician and a gynecologist where cryotherapy and LEEP services are offered. The Pap smear is collected by a trained female health assistant in the maternal and child health unit. The smear is collected using Ayre's spatula and spray fixed (prepared using 5ml polyethylene glycol and 200 ml 95% alcohol). The slides are sent to the Samtse hospital where the cytology-technicians screen for any abnormal or pre-malignant cells. The classification of Pap smear is done according to Bethesda classification system. The slides suspected to have abnormal cells or malignancies are sent to Referral Hospitals for further confirmation by the pathologist. The patients with low grade malignancy undergo colposcopy and Loop Electrosurgical Excision Procedure (LEEP) in centers with gynecologists.

There are scarce data on Pap smear in Bhutan due to paucity of research on this subject. Except for few studies on knowledge, attitude and practice on Pap smear and factors associated with opting out for screening, there are no studies conducted to estimate the abnormality of Pap smear. The study objective was conducted to estimate the abnormal slide rate and identify the factors associated with abnormal Pap smear in Samtse Dzongkhag.

Materials and Methods

Study design and setting
This was a retrospective cross-sectional study involving review of medical records maintained in the cytology unit of Samtse General Hospital.

Study population
All women who had received Pap screening services in BHUs and hospitals of Samtse District in the year 2018 were included in this study.

Data Sources and collection
The data was initially extracted from the Pap smear request form to pro-forma and later entered into epi data.

Study variables
The variables used to check for associations were age of women, age at marriage, age at first pregnancy, number of sexual partners, number of children, history of sexually transmitted diseases and presence of symptoms.

The dependent variables were divided into normal Pap smear (examination of the smear slide was normal) and abnormal smear (Abnormal cells such as ASCUS, LSIL, HSIL or frank malignancy were seen in the smear).

Data Management and Analysis
The data was double entered in epi data version 4.4.3.1. and analyzed using Stata version 12. Descriptive statistics is presented as mean, frequency and percentage. Chi square test and fisher test were used to assess the statistical association keeping a p-value of <0.05 as statistically significant.

Ethical clearance
The ethical clearance was taken from the Research Ethics Board of Health (REBH) of Ministry of Health, Bhutan. Since, this is a retrospective study and doesn't involve direct interaction with the participants, waiver for written inform consent was sought from the REBH. Patient confidentiality was maintained by removing all personal identifiers and assigning a unique code on the pro-forma, which was kept under lock and key. The electronic data files are protected by computer by use of password and shared only with the study team members.

Results

During the study period, 1993 women availed Pap smears from the cytology units of Samtse Districts. The mean age was 37.9 years. The majority of women (62%) were in the age group below 39 years. Socio-demographic characteristics are presented in Table 1. Over half (56.65%) of the participants were housewives by occupation and majority (87.51%) of them were sexually active. Ninety three percent of the participants have ever had one sexual partner and

Table 1. Socio - Demographic Characteristic (n=1993)

Variables	Frequency	Percent
Age (years)		
<30	457	22.9
30-39	784	39.3
40-49	438	22
>50	314	15.8
Occupation		
Farmer	574	28.8
Housewife	1129	56.7
Armed force	4	0.2
Civil servant	153	7.7
Private service	44	2.2
Business	63	3.2
Corporations	24	1.2
Others	2	0.1
Sexual activity		
Not active	4	0.2
Presently active	1744	87.5
Formally active	245	12.3
Sexual partner ever had (n:1984)		
1	1856	93
2	119	6
>=3	9	0.5
Contraception		
Nil	858	431
Barrier	178	8.9
OCP	164	8.2
DMPA	319	16
IUD	45	2.3
TL/VO	429	21.5

43% of them did not use contraception.

History of marriage and pregnancies is presented in Table 2. Most (92.22%) of the participants were currently married and around 10% of have been married more than once. Around 7% of them were married before they attained 15 years of age and 16% of them had their first pregnancy before the age of 18 years.

Clinical Characteristic

Almost all (98.90%) the participants did not have past history of sexually transmitted infections (STI) and around one-third of them had undergone a previous Pap-smear test (Table 3). Around 6% had past history of inter-menstrual bleeding and 4% had history of cervical erosion. The majority (97.49%) of the slides were normal. 18 (0.9%) of patients had ASCUS and 9 (0.45%) had HSIL. Of the total number of smears taken, 2.5% (47) were found to be abnormal. Two patients aged more than 45 years also had squamous cell carcinoma.

In bivariate analysis using chi square and fisher exact test (Table 4), the abnormal Pap smear was significantly associated with marital status and age (p-value < 0.05).

Discussion

This study presents the first data on the performance of Pap smear in a large district of Bhutan which has the potential to be representative of the country. In this study, the slide abnormality rate of Pap smear in Samtse District was 2.5% in 2018. This is comparable to a study in Turkey [15] where the slide abnormality rate was 2.5% and 4.7% [16]. However, this is much lower than a study in India, where slide abnormality was as high as 72.5% [17]. In another study in India, the cell abnormality rate was 10.8% [18]. These differences among countries and regions could be due to difference in culture, race [19], HPV prevalence and sexual behaviors among this countries. Although, Bhutan is generally open society with more than half the population engaged with multiple sexual partners [20], the abnormal Pap smear is still low. This could be due to use of condom outside one's marriage. An important contribution to these differences

Table 2. History of Marriage and Pregnancy (n=1993)

Variables	Frequency	Percent
Single	32	1.6
Married	1838	92.2
Divorced	56	2.8
Widow	67	3.4
No. of marriages (n: 1973)		
1	1809	91.7
2	151	7.7
≥ 3	13	0.7
Age at first marriage (n:1975)		
<15	149	7.5
15-19	1025	51.9
20-24	637	32.3
25-29	146	7.4
≥ 30	18	0.9
No of marriages of husband (1940)		
1	1751	90.3
2	168	8.7
≥ 3	21	1.1
No of pregnancies		
No pregnancy	95	4.8
1-2	933	46.8
3-4	723	36.3
>4	242	12.1
Age at 1st pregnancy		
<18	328	16.5
18-28	1497	75.1
29-38	69	3.5
>38	99	5
Last delivery/abortion (year) (n=1640)		
≤5	544	33.2
5.1-10	362	22.1
10.1-15	259	15.8
15.1-20	219	13.4
20.1-25	160	9.8
>25	96	5.9

could be the expertise of the technicians screening the smears in microscopy. All smears in this study were screened by technicians and not qualified Pathologists. Although these are trained cyto-technicans, their limited expertise may result in misinterpretations. However, in such a scenario it is more likely to have more abnormal findings since technicians would probably grade doubtful slides as abnormal rather than normal. The most common abnormality in this study was ASCUS. This was a similar finding in other studies as well [16-21].

The majority of those availing the services in our study were women in the reproductive age groups. This could be due to better awareness on Pap smear services among younger women who are sexually active. The women in reproductive age groups are usually better informed about such screening services due to recurrent exposures to health workers during the time of antenatal, post-natal services and family planning services. This trend is similar in other countries as well [22]. Housewives received Pap smear screening compared to other occupational groups. This was a similar finding in the capital city of Thimphu as well [23]. The main reason could be due to the availability to time for these housewives to avail the services than those with permanent employment.

In this study, the abnormal Pap smear was significantly associated with the married women. HPV is responsible for majority of cervical cancer and it is sexually transmitted [2]. Multiple studies in other countries have

Table 3. Clinical Characteristic (n=1993)

Variables	Frequency	Percent
Past history of STD		
0	1971	98.9
1	15	0.8
2	7	0.4
Previous Pap smear test		
Yes	664	33.3
No	1329	66.7
Past history of Inter-menstrual bleeding		
Yes	116	5.8
No	1877	94.2
Past history of post-coital bleeding		
Yes	23	1.2
No	1970	98.9
Past history of contact bleeding		
Yes	99	5
No	1894	95
Past history of cervical erosion		
Yes	89	4.5
No	1904	95.5
Present history		
Discharge present	119	6
Bleeding present	15	0.8
Pruritis present	3	0.2
lower abdominal pain present	17	0.9
No symptoms	1839	92.3
Pap smear type		
Normal	1943	97.5
ASCUS	18	0.9
LSIL	8	0.4
ASC-H	8	0.4
HSIL	9	0.5
LSIL-HPV	2	0.1
Polyp	3	0.2
SCC	2	0.1

shown that multiple Pap smear is protective of cervical cancer. The pre-malignant lesions take years to become malignant lesion. Moreover, Pap smear which is the most common screening test used in developing countries has sensitivity of only 55.7% due to which a single test may not be able to detect the malignant lesions [5].

In this study, two patients had developed squamous cell carcinoma who were both older than 45 years. One of these patients never had Pap smear done and was detected when she presented with bleeding per vaginal. The most common symptoms of cervical cancer is bleeding per vaginal [24].

The use of condom prevents transmission of sexually transmitted infections due to which the incidences of abnormal Pap smear decreases [25-26]. However, in this study there was no difference in Pap smear among users

and non-users of condom. The difference in result could be due to the setting of the questions in the form. The use of contraception in our data indicates the use of barrier method at the time of Pap smear screening.

The risk factors for cervical cancer include (but not limited to) sexually transmitted infections (HPV, chlamydia trachomatis and HIV), multiple sexual partners, high parity, OCP use, obesity and smoking [27-29]. Studies have shown that regular screening in women decreases cervical cancer by 67% [30]. A systematic review showed that screening for cervical cancer by any method is associated with decreased incidence and death from cervical cancer [31]. The mortality associated with cervical cancer can be prevented by timely access to comprehensive cervical cancer prevention and control program which advocates for HPV vaccination for girls

Table 4. Association between the Independent and Dependent Variables

Variables	Normal smear		Abnormal smear		p-value
	Frequency	Percent	Frequency	Percent	
Age (years)					
<=45	1514	77.8	30	63.8	0.023
>45	432	22.2	17	36.2	
Occupation					
Farmer	562	28.9	12	25.5	0.287**
Housewife	1100	56.5	29	61.7	
Govt/ corporations/ armed forces	177	9.1	6	12.8	
Business/ private	107	5.5	0	0	
Marital status					
Single	30	1.5	2	4.3	0.049**
Married	1793	92.1	45	95.7	
Divorced/ widowed	123	6.3	0	0	
Number of marriages					
0	19	1	1	2.1	
1	1766	90.8	43	91.5	0.553**
>1	161	8.3	3	6.4	
No of marriages of husband					
1	1708	90.2	43	93.5	0.33**
>1	186	9.8	3	6.5	
No of pregnancies					
0	93	4.8	2	4.3	0.054**
1-3	1403	72.1	27	57.5	
>3	450	23.1	18	38.3	
Age at 1st pregnancy (n=1895)					
<20	713	38.5	21	46.7	0.408**
20-34	1129	61	24	53.3	
>=35	8	0.4	0		
Sexual activity					
Not active at all	4	0.21	0	0	0.155**
Presently active	1707	87.7	37	78.7	
Formally active	235	12.1	10	21.3	
Sexual partner ever had					
1	1811	93.5	45	97.8	0.362
>=2	127	6.6	1	2.2	
Age at first marriage (years)					
<15	146	7.6	3	6.7	0.23
15-19	995	51.6	30	66.7	
20-24	629	32.6	8	17.8	
25-29	142	7.4	4	8.9	
≥ 30	18	0.9	0	0	
Contraception					
Nil	834	429	24	51.1	0.94
Barrier	175	9	3	6.4	
Others	161	8.3	3	6.4	
Previous Pap smear					
Yes	650	33.4	14	29.8	0.643
No	1296	66.6	33	70.2	

Continued Table 4.

Variables	Normal smear		Abnormal smear		p-value
	Frequency	Percent	Frequency	Percent	
Last delivery/abortion (year)					
≤5	534	33.4	10	25	0.321
5.1-10	353	22.1	9	22.5	
10.1-15	250	15.6	9	22.5	
15.1-20	210	13.1	9	22.5	
20.1-25	158	9.9	2	5	
>25	95	5.9	1	2.5	

**Fisher test

and screening and treatment for pre-cancerous lesion [8].

Since Bhutan has embarked on the elimination of the cervical cancer during the 144th session of WHO executive board at Geneva [32], the provision of quality and timely results for Pap smear needs to be strengthened. Unlike most cancers, the elimination of cervical cancer is doable since, it has a long latent period. Therefore, the Pap smear screening at earlier age can detect pre-malignant lesions and can be treated appropriately before it becomes malignant. However, the older women should not be neglected as high prevalence of abnormal cytology in Pap smear has also been observed in older women too [33]. This further reiterates the need for equitable continued Pap smear screening both young and old women.

This study has its own limitations. Since this was a retrospective study, other factors which could affect the Pap smear report like education and income couldn't be accessed. Moreover, the Pap smear services are offered passive screening whereby women with abnormal smears may not have come forward for screening services. Other risk factors like intake of alcohol and tobacco was not accessed in this study.

In conclusion, the study found that slide abnormality rate of 2.5% in Samtse District. The abnormality is more common among married and older women. Therefore, additional screening efforts needs to be more prioritized on this group to detect pre-malignant lesions. Since Bhutan has embarked for elimination of cervical cancer, additional screening camps needs to be carried out to reach the unreached. And the health assistants in the BHU needs to be properly trained and motivated to achieve this goal.

Declaration of interest

There is no conflict of interest involved for this study.

Financial disclosure

There is no budget involved in this study.

Author's contribution

All the authors contributed equally for the conception, drafting, analysis and finalization of the manuscript.

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