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Awareness and Practice of Pap Smear among Female Hospital Workers in Abia State University Teaching Hospital Aba South East Nigeria

L. Uche Chika^{1*}, C. Ekeleme Ngozi², C. Iwuoha Ejiro² and J. Awa Madu²

¹Department o f Hematology, Abia State University Teaching Hospital, Aba, Nigeria. ²Department of Community Medicine, Abia State University Teaching Hospital, Aba, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author UC designed the study, wrote the protocol, performed some aspects of the statistical analysis, did the literature search and wrote the first draft of the manuscript. Authors EN contributed in the study design, collection of data and in proof reading the manuscript. Author IE also contributed in the study design, data collection, did some literature search, managed statistical analysis of the study. Author AM helped in data collection and in the proof reading of the manuscript. All authors read and approved the final manuscript.

Article Information

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Original Research Article

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ABSTRACT

Background: Cervical cancer is the fourth most common cancer in females worldwide and the commonest cancer in the female genital tract. Early detection is critical in the diagnosis.

Objective: To determine the awareness and practice of pap smear among female health workers in Abia State University Teaching Hospital (ABSUTH).

Method: This was a cross-sectional descriptive study conducted among female hospital staff of (ABSUTH), About 150 questionnaires were administered out of which 124 responded giving a response rate of 82%. Data was analyzed using SPSS version 20.

Result: A total of 124 female workers; 76(61.3%) health workers and 48(38.7%) support staff participated in this study. Their mean age was 40.7 ±8.7 years. About 76(61.3%) of the respondent

had heard of pap smear. However more than half of them 64(52.4%) were not aware that pap smear was being done in ABSUTH. Only 14(11.3%) of the respondents had done Pap smear previously. There was a statistically significant association between cadre of staff and awareness of pap smear (P < 0.001) in addition, health workers were about 4 times more likely to have ever heard of pap smear than support staff (OR 3.92, 95% CI 1.812- 8.45 P 0.00) **Conclusion:** The study observed a fair awareness and very poor practice of pap smear among female hospital staff who ought to be at the forefront in enlightening their environment.

Keywords: Awareness; practice; pap smear; female; hospital workers.

1. INTRODUCTION

Cervical cancer is the commonest cancer in the female genital tract [1-4]. There are two types of cervical cancer: Squamous cell cancer and adenocarcinoma. About 80 to 90 % of cervical cancers are squamous cell cancers while 10 to 20% are adenocarcinoma [4]. The incidence of cervical cancer has declined drastically in the developed world, due to wide availability of screening, unlike what is obtainable in developing nations. Globacom 2012 estimated that cervical cancer is the fourth most common cancer affecting women globally, after breast, colorectal, and lung cancers, and also the fourth most common cause of cancer death. [5] Globally, cervical cancer is diagnosed annually in over 500,000 women and it is known to account for 270, 000 deaths, about 88% of which occur in developing countries; 53,000 in Africa; 31,700 in latin America and the Carribean and 159,800 in Asia [6,7]. In United States, more than 12,000 women were estimated to be diagnosed with cervical cancer and more than 4,000 deaths annually[4]. In Africa, about 78,922 new cases were seen globally out of which 61,070 death occurred with case fatal rate of 78.1. The highest case load of cervical cancer is in Eastern African region 43% and lowest is West Africa 9.8% [6]. In 2007, it was reported that 36.59 million women aged ≥15 years in Nigeria are at risk of developing cervical cancer. In 2010, the World Health Organization reported that 9,922 women were diagnosed annually with cervical cancer in Nigeria out of which 8,030 die of the disease [6].

Most cervical cancers are caused by HPV infection with two prominent types, (16 and 18) which are responsible for about 70% of all cases. Human papilloma virus (HPV) prevalence is 24.8% [8]. Current vaccination programmes cover types 16 and 18, which is reported to prevent 66.2 % of cervical cancers [9]. Prevention can be achieved by immunizing young girls between the ages of 9-16 (before the age of sexual debut). Mothers are becoming increasingly aware of this vaccine and its importance in the lives of their children, however, uptake is low due to cost [10].

National cancer coalition 2008 discovered that the main reason for the high incidence of cancer resulted from lack of effective screening programs [4]. Cervical cancer is known to be one of the most preventable cancers amongst others. Death from cervical cancer has declined by approximately two percent per year in the United States since the knowledge of prevention improved [5]. Similarly deaths from cervical cancer have fallen over the last 20 years in the United Kingdom and the reduction is mainly due to the National health service cervical screening programme, which may detect changes in the cells of the cervix at a precancerous stage [4].

There are different screening programmes that can be used to detect the precancerous changes so as to prevent the development of the diseases and curb its serious consequences. Some of these screening programmes include; visual method such as Pap smear or visual inspection with acetic acid (VIA), visual inspection with Lugol's iodine (VLI), care Human papilloma virus (care- HPV) and HPV-DNA based screening among others.

American Cancer Society 2012 recommends that all women should begin cervical screening ate 21 years; a 3 year interval can be considered in the age group 21 to 29 years. Between 30 – 65 years women should have pap test and HPV test every 5years or preferably, to have pap smear every 3 years. Women who have had the HPV vaccine should follow the screening recommendations for their age group [11].

National Cervical Cancer Coalition 2008, estimated that only 5% of women in Nigeria had been screened for cervical dysplasia in the past 5 years compared with 40 - 50% seen in developed countries [5].

Previous works done discovered that most women in Nigeria presented with advanced

disease where radiotherapy had little benefit and hysterectomy of no benefit; Majority of the patients presented in stages III and IV in the following studies; more than 56.0% in Ebonyi state [12]; less than 75.0% reported from Rivers [13] while 85.5%, 86.0%, 78.6%, and 89.3%, from Zaria, Abuja, Sagamu, were given for late presentation which include: lack of awareness of cancer Nnewi respectively [14-17]. Various reasons symptoms, seeking after alternative care, fear of diagnosis and the challenges of distance to available centers of treatment [18]. Poverty and/or widowhood, early marriage, polygamy, grand multiparity, and illiteracy have all been found to be significantly associated with increased risk of occurrence of cervical cancer and could contribute to the high incidence of late presentation [19].

Early detection is critical in the diagnosis of cervical cancer as precancerous cervical cell changes and early cancers of the cervix generally do not cause symptoms. For this reason, regular screening through Pap smear can help catch precancerous cell changes early and prevent the development of cervical cancer.

Pap smear is a cytological screening test with proven efficacy in reducing cervical cancer incidence and mortality. A study by Gustafsson et al showed that incidence of cervical cancer was reduced by as much as 90% with a very effective screening program [20].

Studies conducted in the Northern part of Nigeria showed fair knowledge, good attitude but poor practice of cervical cancer screening amongst the market women [21]. Similar situation was found even amongst health workers in a study conducted in Enugu South East Nigeria [22]. There is paucity of information regarding the knowledge of cervical cancer, attitude and practice of Pap smear in our environment, hence the need for this study.

2. METHODOLOGY

This was a cross-sectional study conducted among female hospital staff of Abia state university teaching hospital (ABSUTH). ABSUTH is a tertiary healthcare institution located in Aba, south east Nigeria. It has a total of 894 staff including 618 females and 276 males. Among the female staff, were 338 health workers and 280 support staff.

The study included all consenting female staff; exclusion criteria included those on leave and

those that did not give their consent to participate. The female workers were categorized into two groups; health workers and support staff. Health workers included; Doctors, Nurses, Scientist Pharmacist, laboratory and Physiotherapist. Support staffs included; administrative staff, technical staff, security and ward orderlies. Participants were selected proportionately from various cadres of staff through simple random sampling of each cadre.

Data were collected using semi-structured self administered questionnaire after obtaining an informed consent from the respondents. The questionnaire was developed by the researches from previous studies [23,24,25]. The questionnaire was pretested to assess validity and reliability and necessary adjustment made before administration. Data was collected between 1st and 30th October 2016.

The questionnaire obtained information on sociodemographics, including; age, marital status, number of children, occupation and number of work years in the institution.

Information was also obtained on the following; haven heard of Pap smear, sources of information, what Pap smear is used for, uptake of the screening services, the last time pap smear was done, reasons for not doing it, symptoms of cervical cancer, knowledge of availability of Pap smear in the institution and previous enlightenment on Pap smear. Information on correct age for pap-smear was also sought from respondents.

Ethical committee of Abia State University Teaching Hospital reviewed and approved the study protocol.

Data were entered and analyzed using SPSS version 20, qualitative variables were summarized as counts and percentages while Chi-square and logistics regression were used for associations and p<0.05 was considered statistically significant.

3. RESULTS

A total of 160 women were recruited and questionnaires were administered out of which 124 were correctly filled and returned, giving a response rate of 82%. The mean age of the respondents was 40.7 \pm 8.7 years, One hundred and two (81.5%) were married, 17(13.7%) were single while 6(4.8%) were widowed. (Table 1). Health workers constituted 76(61.3%) while

48(38.7%) were support staff. Majority 70(56.5%) of the workers had worked for more than 10yrs while 54(43.5%), had worked for less than 10yrs.

About 76(61.3%) of the respondent had heard about pap smear while 48(38.7%) had not heard. (Table 2). About 43(56.6%) got the information about pap smear from the hospital; 10(7.6%) heard about it from television; 6(7.9%) from free screening programme; 4(5.6%) from friends while 13(17.1%) did not specify their source of information. Among the respondents, 75(60.5%) knew about what pap smear was used for; 20(16.1%) were not sure while 29(23.4%) did not know. In terms of enlightenment on Pap smear, only about 13(10.5%) had received formal enlightenment while 111(89.5%) had not. Moreover, more than half of the respondents 64(52.4%) were not aware that pap smear was done in ABSUTH. Only 40(32.3%) of the respondent knew the age at which a woman should start doing Pap smear. While 73(67.7%) did not know (Table 2).

In terms of the practice of pap smear, only 14(11.3%) of the respondent had done Pap

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smear previously while 110(88.9%) of the respondent had not. For respondents that had not done pap smear, about 68(61.8%) gave no reason for not doing it, 20(18.2%) felt it was not necessary, 14(12.7%) couldn't due to of lack of finances while 8(7.3%) were afraid of discovering cancer (Table 3b).

Table 1. Socio-dermographic characteristics

Parameter (n=124)	Frequency	Percentage
		(/0)
Age		
<40	59	47.6
40yrs &above	65	52.4
Marital status		
Single	17	13.7
Married	101	81.5
Widowed	6	4.8
0ccupation		
Health workers	76	61.3
Support staffs	48	38.7
Work experience		
<10years	54	43.5
10years and above	70	56.5

Parameter	Frequency(n=124)	Percentage (%)
Ever heard of pap smear		
Yes	76	61.3
No	48	38.7
Sources of information		
Hospital	43	56.6
Television/radio	10	7.6
Friends	4	5.6
Free screening program	6	7.9
Others	13	17.1
Pap smear is used to detect precancerous		
growth		
Yes	75	60.5
No	20	16.1
Not sure	29	23.4
Age for starting pap smear		
21-30years	40	32.3
31-40years	36	29
41-50years	17	13.7
Above 50 years	1	0.8
Don't know	16	12
Formal enlightenment on pap smear		
Yes	13	10.5
Νο	111	89.5
Is pap smear done in the ABSUTH?		
Yes	59	47.6
No	64	52.4

Table 2. Awareness of pap smear amongst absuth workers

Table 3a. Practice of pap smear among female absuth workers

Variable	Frequency	Percent
Ever done pap		
smear before		
Yes	14	11.3
No	110	88.7
Last time pap smear		
was done		
0-6month	4	28.6
7-12month	2	14.3
1-2 years	3	21.4
>2years	5	35.7

 Table 3b. Respondent's reason for not doing pap smear

Parameters	Frequency n=110	Percentage (%)
Not necessary	20	16.1
Don't have	14	13.3
money		
Fear of discovery	8	6.5
cancer		
No reason	68	66.1

Table 4. Symptoms of cervical cancer among respondents

Ever had Irregular Bleeding		
Yes	2	1.6
No	122	98.4
Ever had vaginal pain		
Yes	3	2.5
No	121	97.5
Ever had foul smelling vaginal discharge		
Yes	2	1.6
No	122	98.4

There was a statistically significant association between cadre of staff and awareness of pap smear (x^2 = 12.71, P < 0.001) while no statistical significant association was found between age of staff, marital status, working experience and awareness of pap smear (Table 4) Logistic regression showed that the health workers were about 4 times more likely to have ever heard of pap smear than support staff (OR 3.92, 95% CI 1.812- 8.45 P 0.00). Table 5 shows the association between sociodermographic characteristics and awareness of Pap- smear. There was a statistically significant association between cadre of staff and awareness of pap smear while no significant association was found between age of staff, marital status, working experience and awareness of pap smear.

4. DISCUSSION

The knowledge of cervical cancer screening and the detection of pre - cancerous leision is fundamental to the prevention to this cancer. This study showed a fair knowledge of cervical cancer screening with pap smear as 61.3% of the respondent were aware of pap smear. This finding is in keeping with an Indian study by Agam B et al [25], where 65.5% of the participants were aware of pap smear. Higher level of awareness was also discovered by studies done in Lagos [26] and Sokoto [27] among the knowledgeable health workers. However, previous study done in this environment among women in Aba by Feyi-Waboso et al reported only 16% [28].The difference in level of awareness between this study and our findings can be attributed to the fact that majority of our respondents were health workers. Hospital was the major source of information of pap smear among these respondents. While the major sources of information from Sokoto study [27] (among nurses) were classroom and seminar whereas the source of information of Lagos study [26] (amongst the health workers) was electronic media. These explain the environmental impact on disseminaton of information.

About 60.5% of the respondents were aware that pap smear is used to detect precancerous changes in the cervix however only 32.5% of the respondents had a correct knowledge of the age to start pap smear. This is close to the results obtained in another study [29]. where 55.7% were aware that pap smear was used to detect premalignant lesion. Among the respondents, only 13(10.5%) had received a formal enlightenment, and this explained why majority (52.4%) of the participants had no knowledge of pap smear being done in our hospital. This showed a knowledge gap among the staff about laboratory services available in the hospital. Therefore, staff enlightenment and orientation is needed to bridge this gap.

Parameters	Heard of pap	Not heard of pap	Chi- square	p-value
	Frequency (%)	Frequency (%)		
Age				
<40	33(55.9%)	2.6(44.1%)	0.24	1.36
40yrs &above	43(66.2%)	22(33.8%)		
Occupation				
Health workers	56(73.7%)	20(26.3%)	12.71	0.001*
Support staff	20(41.7%)	28(58.3%)		
Marital status				
Single	11(64.7%)	6(35.3%)	5.30	0.07
Married	64(63.4%)	37(36.6%)		
Widowed	1(16.7%)	5(83.3%)		
Work experience	. ,			
<10years	32(59.3%)	22(40.7%)	0.68	0.16
10years and above	44(62.9%)	26(37.1%)		
	+O*	atistically significant		

Table 5. Association between socio-dermographic parameters and ever heard of pap smear

Statistically significant

The practice of pap smear amongst the respondent was generally poor as only 11.1% had ever accessed it before. This finding agreed with aforementioned studies done in this environment [28] and another study [30] done in Enugu amongst certified nurses where only 16% and 12.2% respectively had done pap smear. The story is not different in India, where there has been well established national cancer program, as only 9.5% of the participants had undergone pap smear screening [25]. The situation in the United States of America is totally different as tremendous amount of effort had been devoted into cancer screening, a study on frequency of pap smear amongst American women estimated that 61 million women had at least one pap smear in the year 2000[31]. This study also reported that majority of the women were being screened annually.

Majority of the respondents (66.1%) who had not done pap smear gave no reason, (Table 3b) some respondents (16.1%) felt it was not necessary, some gave financial reasons while few others, fear of discovering cervical cancer. Generally, the reason for not doing pap smear may be alluded to the fact that majority (97%) of the respondents did not have symptoms associated with cervical cancer. This finding buttresses the fact that preventive care is still a major issue in our environment as people wait for symptoms of a disease to occur before taking action. The attitude of the respondents to pap smear is similar to that observed by Ajibola Idowu et al who found that low risk perception was the main reason attributed to non screening of most of the

respondents who had never been screened [32]. There was a statistically significant association between cadre of staff and awareness of pap smear (x^2 = 12.71, P < 0.001) while no statistical significant association was found between age of staff, marital status, working experience and awareness of pap smear (Table 4) The study showed that the health workers were about 4 times more likely to have ever heard of pap smear than support staff (OR 3.92, 95% CI 1.812- 8.45 P 0.00). This supports the facts that by reason of their academic background health workers are better enlightened and are more knowledgeable than support staff. The Sokoto study by Ochei et al also found no statistically significant association with uptake of Pap smear. This observation was different from that of a Jamaican study[33]. where married women were found to be two times more likely to have had a Pap smear than single women.

5. CONCLUSION

The study observed a fair awareness and very poor practice of pap smear among female hospital staff who ought to be at the forefront in enlightening their environment. Ignorance of the availability of the pap smear in the hospital laboratory may have contributed to poor practice of this test among the respondent. Therefore, more awareness and enlightenment on pap smear are needed in the hospital and beyond to help in detecting pre-malignant leision, offer preventive measure and ultimately curb the menace of cervical cancer.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Okeke TC, Onah N, Ikeako LC, Ezenyeaku CCT. The frequency and pattern of female genital tract malignancies at the University of Nigeria Teaching Hospital, Enugu, Nigeria Ann. Med. Health Sci. Res. 2013;3:345-8.
- Galadanci HS, Mohammed AZ, Uzohota O, Chicha O. Gynaecological malignancies seen in tertiary health facility in Kano Northern Nigeria. Trop J Obstetgynae. 2003;20:105-108.
- 3. Jedy-Agba E, Curado MP, Ogunbiyi O, et al. Cancer incidence in Nigeria: A report from population-based Cancer Registries. Cancer Epidemiol. 2012;36;5:271-8.
- 4. National cervical cancer coalition (NCCC); 2008.
- 5. GLOBOCAN. Cancer Incidence and Mortality Worldwide; 2012.
- World Health Organization. Comprehensive cervical cancer control: A guide to essential practice. Screening for cervical cancer. Geneva, WHO Press; 2002.
- 7. Globocan. Cancer incidence, mortality and prevalence worldwide. International Agency for Research on Cancer; 2008.
- WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papilloma virus and Related Cancers in Nigeria.Summary Report 2010. Geneva. World Health Organisation; 2010.
- 9. Cancer N Institute. Cancer Advances Infocus Cervical Cancer; 2013.
- 10. Ogochukwu TN, Akabueze J, Ezeome IV, Aniebue UU, Oranu EO. Vaccination

against Human Papilloma Virus in Adolescent Girls: Mother's Knowledge, Attitude, Desire and Practice in Nigeria. J Infect Dis Preve Med. 2017;5:151. DOI:10.4172/2329-8731.1000151

- 11. American Cancer Society. 2012.
- Eze JN, Emeka-Irem EN, Edegbe FO. A Six-Year Study of the Clinical Presentation of Cervical Cancer and the Management Challenges Encountered at a State Teaching Hospital in Southeast Nigeria. Clin Med Insights Oncol. 2013;7:151-158.
- 13. A 13- year clinico-pathological review. Niger J Med. 2004;13(2):110-3.
- 14. Oguntayo OA, Zayan M, Kolawole AO, et al. Cancer of the cervix in Zaria, Northern Nigeria Ecancermedicinalscience. 2011;5:219.
- Umezulike AC, Tabansi SN, Ewunonu HA, Nwana EJ. Epidemiological characteristics of carcinoma of the cervix in the Federal capital Territory of Nigeria. Niger J Clin Pract. 2007;10(2):143-6.
- Olatunji AO, Sule-Odu AO. Cancer of the cervix. Niger Postgrad Med J. 2005;12(4):308-11.
- Ikechebelu JI, Onyiaorah IV, Ugboaja JO, Anyiam DC, Eleje GU. Clinicopathological analysis of cervical cancer seen in a tertiary health facility in Nnewi, south-east Nigeria. J Obstet Gynaecol. 2010;30(3): 299-301.
- Oladeji A, Atalabi O, Jimoh M, Ntekim I, Elumelu T. Delay in presentation of cancer patients for diagnosis and management: An institutional report. The Internet Journal of Oncology. 2016;13:1.
- Ketiku KK, Ola ER, Ekanem EE. Cancer of the cervix in Nigeria: A case-control study of some epidemiological factors. NQJHM. 2004;14(2):161-5.
- Gustafsson L, Ponten J, Zack M, Adami HO. International incidence rates of invasive cervical cancer after introduction of cytological screening. Cancer Causes Control. 1997;8:755-763.
- Ahmed SA, Sabitu K, Idris SH, Ahmed R. Knowledge attitude and practice of cervical cancer screening among market women I Nigeria. Niger Med J. 2013;54:316-9.
- 22. Ayinde OA, Ogunbode OO. Determinants of cervical cancer knowledge and its utilization of screening among a Nigerian female population. Trop J Obstet Gynae. 2005;22:21-4.
- 23. Kress CM, Sharling L, Owen-Smith AA, Desalegn D, Bloomberg AM, Goedken T.

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Knowledge, attitudes, and practices regarding cervical cancer and screening among Ethiopian health care workers. Int J Womens Health. 2015;7:765-772.

- 24. Ehiemere IO, Frank MD, Robinson-Bassey GC. Attitude and practice of cervical cancer screening among female health workers in university of Port-Harcourt teaching hospital, Rivers State. Journal of Research in Nursing and Midwifery. 2015;4(5):72-82.
- Oche MO, Aoje AU, Gana G, Ango JT. Cancer of the cervix and cervical screening: Current knowledge, attitude and practices of female health workers in Sokoto, Nigeria 2013. International Journal of Medicine and Medical Sciences. 2013;5(4):184-190.
- Agam BB, Abhijit PP, Neelkamal K, Ragini M, Arun MK. Knowledge, attitude, and practices related to cervical cancer among adult women: A hospital-based crosssectional study. J Nat Sci. Biol. Med. 2015;6:2:324-328.
- Awodele O, Adeyomoye AA, Awodele DF, Awodele IO, Dolapo DC. A study on cervical cancer screening amongst nurses in lagos university teaching hospital, Lagos, Nigeria. J. Cancer Educ. 2011;26(3):497-504.

- Feyi-Waboso PA, Kamanu C, Aluka C. Awareness and risk factors for cervical cancer among Women in Aba, southeastern Nigeria. Tropical Journals of Obstetrics and Gynaecology. 2005;22.
- 29. A dissertation Submitted in partial Fulfillment of the Requirement for the Degree of Master of Medicine (Obstetrics and Gynecology) University of the Muhimbili of Health and Allied Sciences Muhimbili.
- Nwankwo KC, Aniebue UC, Agwuna KK. Cervical cancer screening among certified nurses in Enugu: Knowledge, Attitude and Uptake of Pap Smear Test. International Journal of Medicine. 2010;5;1.
- Brenda E. Sirovich, Gilbert H. Welchi the frequency of pap smear screening in the United States. J Gen Intern Med. 2004;19(3):243-250.
- 32. Ajibola I, Samuel Aderonke T. Determinants of Cervical Cancer. Screening uptake among women in ilorin, north central Nigeria: A community-based study. Journal of Cancer Epidemiology. 2016;8.
- Buthol N, Amita B, Jeremy K, Patricia B, Pauline E. Factors associated with the uptake of cervical cancer screening among women in Portland Jamaica. NAmJ Med Sci. 2015;7(3):104-1.

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