Original Article

Comparison of Papanicolaou Smear Quality with the Anatomical Spatula and the Cytobrush–Spatula: A Single-Blind Clinical Trial

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Abstract

Background: The Papanicolaou (Pap) smear is a standard test for cervical cancer screening; however, the most important challenge is high false-negative results due to inadequate sampling using the Ayres spatula. The cytobrush has been used in combination with the Ayres spatula (cytobrush–spatula) in an attempt to improve the quality of smears with additional costs. The aim of this study was to compare the Pap smear quality with the anatomical spatula (with extended tip) and the cytobrush–spatula. **Materials and Methods:** This was a prospective single-bind clinical trial. One hundred and ten sexually active women aged between 22 and 65 years were randomized into groups, each having two smears at the same time: one with a cytobrush–spatula and another with an anatomical spatula. Fifty-five patients were randomized to have the anatomical spatula first to obtain their smears and 55 were randomized to have the cytobrush–spatula first to obtain their smears. Slides were assessed by a pathologist. **Results:** There was no significant difference in the quality of the smears using the two devices with respect to cellular adequacy ($P = 0.3532$), absent blood staining ($P = 0.7766$), presence of endocervical cells ($P = 0.3502$), and evidence of transformation zone sampling using the Bethesda criteria (0.4028). Kappa analysis shows moderate inter-rater agreement between the two devices by ability to show evidence of transformation zone using British Society for Clinical Cytology and Bethesda criteria. **Conclusions:** There was no significant difference in the quality of smears obtained using the two different methods. The anatomical spatula can be used as a single device in conventional cytology in place of the cytobrush–spatula with the aim of improving the quality of smears without necessarily increasing the cost.

Keywords: Anatomical spatula, cervical cancer, cytobrush–spatula, Papanicolaou smear

Introduction

Cervical cancer is an important women's health problem and a preventable disease of significant public health concern, especially in developing countries where an estimated 190,000 women die from the disease each year.[1]

There were an estimated 527,600 new cases and 265,700 deaths worldwide in 2012. It is the second most commonly diagnosed cancer and the leading cause of cancer death among females in less developed countries.[2]

In Nigeria, cervical cancer is the most common gynecological malignancy and a leading cause of cancer death in women with most cases diagnosed predominantly at advanced clinical Stages III and IV.[3]

Unlike many cancers, cervical cancer can be prevented. It can be prevented using relatively simple and inexpensive technologies to detect abnormal cervical tissue before it progresses to invasive cervical cancer. Cervical cancer prevention worldwide has been based traditionally on screening women using conventional cytology (Papanicolaou [Pap] smear). The overall effectiveness of Pap smear screening programs depends on wide coverage of the target population, quality of smear collection and the appropriate management of abnormal cytology.[4]

To obtain an adequate cervical (Pap) smear, it is necessary to sample the transformation zone (the squamocolumnar junction) from where premalignant change arises.[4]

Over recent years, there has been a tendency for the adequacy of a cervical smear to be judged by the presence or absence of

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endocervical cells since it suggests that the transformation zone, from which premalignant change arises, has been sampled.[5,6] The Report of the Working Party of the Royal College of Pathologists, British Society for Clinical Cytology (BSCC) and National Health Service (UK) cervical screening program recommend that information regarding the presence of metaplastic and/or endocervical cell should be documented as they provide evidence of probable transformation zone sampling.[7]

The sensitivity of cervical screening is limited to some degree by sampling error with false-negative rates varying from 1.5% to 55%.[8,9] Because of false-negative reports, preinvasive diseases are not diagnosed with the eventual development of invasive cervical cancer.[10] Several factors contribute to the incidence of false-negative cases. These include cytological misinterpretation or more likely sampling error due to inappropriate or insufficient number of representative cells obtained or failure of the device or operator to scrape/brush the entire surface of the cervix.[11]

Inadequate smears have been characterized as having insufficient cellularity, being poorly fixed, being contaminated by blood or inflammatory cells or being spread too thickly.[5] Such cervical smears must be repeated to avoid false-negative reports.[12] Many women who develop cervical cancer have had inadequate cytology on previous smears.

Improved cervical sampling will lead to better quality smears and hopefully decrease both false-negative and inadequate smear rates. Therefore, application of the correct tool to prepare the Pap smear should be considered.

Since the Ayres spatula was developed in 1947, it has been widely used, although up to 40% of smears may not contain endocervical cells.[13]

Several other sampling (cell collection) devices have been used to obtain a better yield from the transformation zone.[5] Other commonly used devices include extended tip spatula, cytobrush, and the cervix-brush among others.[14] One of the major drawbacks common to all of them is the inability to adequately sample cells from the transformation zone and endocervix.[14] A Cochrane review focusing on cytological specimen collection devices suggests that the proportion of specimens that are satisfactory for evaluation may be improved by either the cytobrush used in combination with the spatula or the cervix-brush.[15] The cytobrush (used to collect endocervical cells) and wooden spatula (used to collect ectocervical cells) combination involves more steps and consumables.

This study was carried out to compare the quality of smears after sampling with both anatomical spatula and cytobrush–Ayres spatula.

Materials and Methods

Study site and population

The study was carried out among sexually active women aged between 18 years and 65 years attending the gynecology and family planning clinics of the Department of Obstetrics and Gynaecology, Lagos State University Teaching Hospital, Ikeja. Patients were recruited consecutively until the desired sample size of 110 women was attained. The study was conducted over a 4-month period, from September 1, 2015, to December 31, 2015.

Study design

The study was a single-blind prospective clinical trial in which women aged between 18 years and 65 years attending the gynecology and family planning clinics of the Lagos State University Teaching Hospital, were counseled each day to join the study with the aim to enroll 110 participants. Each participant was adequately counseled on the procedure, the implications, significance, her rights and the benefit of participating in the study. They were also briefed clearly on the management options of abnormal smears. A pro forma was used to obtain information about their demographic and other characteristics.

Exclusion criteria

1. Women with ongoing bleeding or menstruation
2. Presence of obvious lesion on the cervix needful of biopsy
3. Pregnant women
4. Women who had undergone hysterectomy or conization
5. Women who were physically and mentally unable to undergo the procedure.

Experimental methods

Two different types of tools were used to take samples from the cervix. The anatomical spatula is a wooden device whose length is 220 mm and its width is 5 mm. This spatula has a long narrow arm with a length 1.7 cm for sampling the endocervix, a shoulder and a completely flat curve for exocervical sampling whose structure is more compatible with women's cervix. The arm of the spatula inserted into the canal while its shoulder was placed in the 3 O'clock position of the exocervix. With gentle pressure, the spatula was rotated in a clockwise direction through 360°. Once the cells were spread on the slide, they were paralleled to the slide edges and the slide was immediately fixed in 90% ethanol.

In the common method of sampling using cytobrush–Ayres spatula, first, the brush is put into the cervix and is rotated through 360° in a clockwise direction and the sample spread on the upper side of the glass slide. Then Ayres spatula wide head is then put on the exocervix and rotated through 360° to obtain sample from the exocervix which is then spread on the lower part of the glass slide and is fixed. The collection devices are depicted in Figure 1.

Sampling procedure

One hundred and ten patients attending the gynecology and family planning clinics who gave their consent were randomized into two groups, each of them having two smears at the same time. The patients were randomized into two groups by picking their own numbers blindly from a box. Those who had even numbers were allocated to have the first smear taken by the cytobrush–Ayres spatula and the second

Figure 1: Collection devices. (a) spatula and cytobrush (b) anatomical spatula

by the anatomical spatula, while those who had odd numbers were allocated to have their first smear taken by the anatomical spatula and the second by the cytobrush–spatula.

Both slides from each patient were numbered only as 1 and 2 and then sent to the cytopathologist. The cytopathologist was thus unaware as to which device was used first for the smear.

The following procedure was designed to take two cervical samples from each participant by the authors to avoid any bias.

First, every participant was made to void urine, then laid down on a couch in a dorsal position and a Cusco's bivalve vaginal speculum was inserted to expose the cervix. A sterile saline-moistened cotton swab was used to wipe excessive cervical discharge.

Then, cervical smears (from both endo- and exo-cervix) were taken by the cytobrush–Ayres spatula and the anatomical spatula, and the order of sampling in each individual was as described above.

The measures of outcome were good-quality smears assessed by evidence of transformation zone sampling based on the presence of metaplastic and endocervical cells and the presence of cervical mucus (E, M and C) according to the BSCC criteria.[7]

The results were also reported based on the Bethesda system[16] using the presence of six groups or more clusters of cells (++ and +++) as evidence of adequate/good quality smears.

Determination of sample size

The incidence rate of cervical cancer in Nigeria is 33/100,000 women. The prevalence rate of 0.033% was used to calculate the sample size for this study using the formula: $n = Z^2 P (1-p)/e^2$, to obtain a minimum sample size of 47.[17,18] We projected a sample size of 110.

Data processing and analysis

The data obtained were entered into the computer and analyzed using the Epi-Info 3.5.3 (January 2011 version) statistical software of the Centre for Disease Control and Prevention Atlanta, USA to generate descriptive statistics. Categorical variables were compared using the Chi-square with Yates correction. Odds ratio and 95% confidence intervals were obtained where necessary. The data were then converted to excel 4.0 and exported to the statistical package for social sciences, version 14.0 (SPSS, inc., 2001, Chicago, IL, USA) to perform inter-rater analysis using Kappa. $P < 0.05$ was considered as statistically significant.

Ethical consideration

Approval for this study was obtained from the Research Ethics Committee of Lagos State University Teaching Hospital, Ikeja. The individuals for the study were fully briefed on the study protocol in a language they understood. They were informed that information gathered will contribute to the knowledge of cervical cancer screening which will go a long way in reducing the incidence of deaths from cervical cancer. They were encouraged to ask questions on any aspect of the study. They were informed of the right of refusal to take part in the study which will not affect the healthcare they are assessing. The women were assured that all information given will be treated as confidential. Benefit of the research was also highlighted which would allow patients to know their current cervical pathology status. They were also informed about the management options of an abnormal smear. Informed written consent was obtained from each participant.

Those whose results were found to be abnormal were referred to the gynecological clinic for appropriate management.

Results

A total of 110 women who gave their consent participated in the study. Each woman had two smears taken using the anatomical spatula and the cytobrush–Ayres spatula. Fifty-five patients were randomized to have the anatomical spatula first to obtain their smears and 55 were randomized to have the cytobrush–spatula first to obtain their smears.

The age of the participants ranged from 22 years to 63 years with a mean of 39.39 ± 9.91 years.

Table 1 shows the assessment of the smear quality as reported by the cytopathologists.

There was no significant difference in the quality of the smears using the two different sampling devices with respect to adequate cellularity ($P = 0.2532$), absent blood staining ($P = 0.7766$), presence of endocervical cells ($P = 0.3502$), and evidence of transformation zone sampling using the Bethesda criteria ($P = 0.4028$).

Table 2 shows the distribution of the110 pairs of smears showing adequate cellularity by type of device. Both devices showed evidence of adequate cellularity in 71 pairs and both showed inadequate cellularity in 9 pairs. It is also evident that 19 pairs of smears showed evidence of adequate cellularity when using the anatomical spatula but did not show such positive result using the cytobrush–Ayres spatula method.

Table 1: Assessment of the smear quality

Characteristics	Anatomical spatula, *n* (%)	Cytobrush spatula, *n* (%)	*P*
Adequate cellularity			
Yes	90 (81.8)	82 (74.5)	0.2532
No	20 (18.2)	28 (25.5)	
Absent blood staining			
Yes	71 (64.5)	74 (67.3)	0.7766
No	39 (35.5)	36 (32.7)	
Presence of endocervical cells			
Yes	86 (78.2)	79 (71.8)	0.3502
No	24 (21.8)	31 (28.2)	
Evidence of transformation zone (Bethesda criteria)			
0-1 group of cells (0)	30 (27.3)	29 (26.3)	0.4028
2-5 (+)	15 (13.6)	18 (16.4)	
6-10 (++)	31 (28.2)	39 (35.5)	
>10 (+++)	34 (30.9)	24 (21.8)	

Table 2: Distribution of smear pairs showing adequate cellularity by type of device

Values are given as *n* and (%)

Anatomical spatula smears showing adequate cellularity	Cytobrush-spatula smears showing adequate cellularity		
	Yes	No	Total (%)
Yes	71	19	90 (81.8)
No	11	9	20
Total (%)	82 (74.5)	28	110

Measure of Kappa agreement: 0.21

This contrasts with just 11 pairs that showed adequate cellularity using the cytobrush–Ayres spatula, but a negative result using the anatomical spatula. Measure of inter-rater agreement using Kappa showed a fair agreement between the two sampling devices ($\kappa = 0.21$). The odds of showing adequate cellularity when using the anatomical spatula is 1.54 that of cytobrush–Ayres spatula with 95% confidence interval of 0.80–2.94.

Adjusting for the order in which a smear was performed with each device does not alter the results as expected since half of the patients were randomized to have one of the devices used first.

Table 3 shows the distribution of the 110 pairs of smears showing evidence of transformation zone (E, M and C) by type of device. Both devices showed evidence of transformation zone in 63 pairs and both did not meet the BSCC criteria in 20 pairs of samples. It is also evident from the table that 10 pairs showed E, M and C when using the anatomical spatula but did not show such a positive result with the cytobrush–spatula. This was in contrast to 17 smears that showed a positive result using the cytobrush–Ayres spatula but a negative result using the anatomical spatula. There is moderate inter-rater agreement between the two sampling devices using Kappa ($\kappa = 0.423$). The odds of showing E, M and C using the anatomical spatula is 1.35 that of the cytobrush–spatula with 95% confidence interval of 0.76–2.41. Adjusting for the order of which the smear was performed first does not alter the result as expected.

Table 4 shows how many of the 110 pairs of smears showed evidence of transformation zone (++ or +++) by type of device using the Bethesda criteria. Both collection devices showed evidence of transformation zone in 48 pairs and both did not show evidence of transformation zone in 30 pairs of samples. From the table, 17 smears showed evidence of transformation zone (++ or +++) when using the anatomical spatula but did not show such a positive result with the cytobrush–spatula. This is in contrast to 15 smears that showed a positive result using the cytobrush–spatula but with a negative result using the anatomical spatula. Measure of inter-rater agreement using Kappa showed fair agreement between the 2 devices ($\kappa = 0.402$). The odds of showing evidence of transformation zone (++ or +++) when using the anatomical spatula is 1.08 that of the cytobrush–spatula with a 95% confidence interval of 0.63–1.84. Adjusting for the order of which the smear was performed first does not alter the result as expected.

Table 5 shows the distribution of the 110 pairs of smears showing the absence of blood staining by type of device. Both devices showed the absence of blood staining in 58 pairs and both showed blood staining in 23 pairs of slides. It is also evident that 13 pairs of the samples obtained using the anatomical spatula showed absence of blood but did not show such positive result when using the cytobrush–spatula. Similarly, 16 slides from the cytobrush-spatula were nonbloody samples but did not show such a positive result with anatomical spatula. Measure of inter-rater agreement using Kappa showed moderate agreement between the two sampling devices ($\kappa = 0.414$). The odds of showing absent blood staining when using the anatomical spatula is 0.89 that of the cytobrush–Ayres spatula with 95% confidence interval of 0.72–1.24. Again adjusting for the order in which a smear was performed with each device does not alter the results as expected.

Discussion

It has been advocated that primary screening should not be carried out with an endocervical brush or Ayres spatula alone as such smears may be composed of endocervical cells or exocervical cells only and may not sample mature squamous cells or transformation zone epithelium.[7] The most effective combination appears to be with the simultaneous use of the cytobrush with an extended tip spatula which is effective in creating high-quality smears and detecting cervical dysplasia.[15] Bountinx reported that using cytobrush alone could not be a suitable method of sampling from exocervical cells, and it should be used along with sharp spatula.[19] The results of the current study demonstrated that similar results can be obtained while sampling by anatomical spatula as well as cytobrush–Ayres spatula.

Taking two smears at the same time for screening may be expensive and cumbersome for routine practice, and therefore,

Table 3: Distribution of smear pairs showing evidence of transformation zone by type of device (British Society for Clinical Cytology criteria)

Values are given as *n* and (%)

Anatomical spatula smears showing evidence of transformation zone	Cytobrush-spatula smears showing evidence of transformation zone (E, M, C)		
	Yes	No	Total (%)
Yes	63	10	73 (66.4)
No	17	20	37
Total (%)	80 (72.7)	30	110

Measure of Kappa agreement: 0.423

Table 4: Distribution of smear pairs showing evidence of transformation zone by type of device (Bethesda criteria)

Values are given as *n* and (%)

Anatomical spatula smears showing evidence of transformation zone (++ or +++)	Cytobrush-spatula smears showing evidence of transformation zone (E, M, C) (++ or +++)		
	Yes	No	Total (%)
Yes	48	17	65 (59.1)
No	15	30	45
Total (%)	63 (57.3)	47	110

Measure of Kappa agreement: 0.402

Table 5: Distribution of smear pairs showing absent blood staining by type of device

Values are given as *n* and (%)

Anatomical spatula smears showing absent blood staining	Cytobrush-spatula smears showing absent blood staining		
	Yes	No	Total (%)
Yes	58	13	71 (64.5)
No	16	23	39
Total (%)	74 (67.3)	36	110

Measure of Kappa agreement: 0.414

a simple single device is highly desirable in busy outpatient clinics. It is imperative that we improve the adequacy of smears in this area of the world without necessarily increasing the financial burden so that women can afford it. Therefore, a collection device that will increase the adequacy of smears without significantly increasing the cost will be highly welcomed so that more women can avail themselves of the test.

The anatomical spatula has the advantage of having a long narrow arm for sampling from the endocervix, a shoulder and completely flat curve for exocervical sampling, thus equivalent to taking two smears in one. The cost implication of one cytobrush spatula is about 2 United States dollars while that of anatomical spatula is about 1 United States dollars.

Using the anatomical spatula, six smears (5.4%) were unsatisfactory or inadequate with no evidence of transformation zone sampling or endocervical cells, compared with 5 (4.5%) with the cytobrush–spatula. These are comparable to the inadequate smear rates reported with the use of liquid-based cytology techniques in various studies with reported rates ranging from 0% to 8.5% with a median of 0.7%.[20]

For a smear to be considered as adequate, sample of cells from the endocervix, transformation zone, and ectocervix must be present in the smear.[21]

Ninety (81.8%) of the smears taken by anatomical spatula had good cellularity compared with 74.5% with cytobrush–spatula, the difference was however not statistically significant.

Using cellular content scores based on the presence of endocervical cells, cervical mucus, and metaplastic cells from the transformation zone to grade the collection of devices performance, the anatomical spatula produced better cellular scores. The idea that the presence of these cells reflects the adequacy of the smear is anatomically plausible since it suggests that the transformation zone from which premalignant change arises has been sampled. The anatomical spatula enables enough endocervix cylindrical cells and exocervix squamous cells to be taken using an easy one step technique.

The Ayres spatula has been widely used for Pap smear but most often associated with unsatisfactory smears as up to 40% of smears may not contain endocervical cells. The presence of endocervical component on the Pap smear is often viewed as a quality indicator of a good Pap smear specimen.[22] In smears

without endocervical cells, any cytological abnormality that is present, especially severe, is less likely to be detected. Assessment of endocervical cells therefore seems to be a valid way to audit the overall quality of a cervical smear screening and to compare different devices.

This study showed that 78.2% of the smears obtained using the anatomical spatula had endocervical cells while 71.8% of those obtained using the cytobrush–spatula had endocervical cells. This difference was however not statistically significant. A study in Shiraz, Iran also comparing the Pap smear quality of the anatomical spatula with that obtained using the cytobrush–spatula also demonstrated a higher percentage of endocervical cells in smears obtained using the anatomical spatula compared to those obtained using the cytobrush–spatula method.[5] Noel[23] in a randomized prospective trial in Houston Texas, USA in 1989 however reported that 90.1% of smears obtained with the cytobrush and Ayres spatula contained endocervical cells compared with only 64.8% in smears obtained with the extended-tip spatula.

Most studies have reported that smears which lack endocervical cells are more likely to carry negative results. Therefore, to minimize the number of false-negative results, the slides must contain enough squamous cells, transitional zone cells and endocervical cells.[21]

We also assessed the quality of the smear pairs by the ability to show evidence of transformation zone using the BSCC criteria and the Bethesda criteria. It is worthy of note that the results using the two criteria were similar. The odds of showing evidence of transformation zone using the anatomical spatula was 1.35 that of the cytobrush–spatula using the BSCC criteria while it was 1.08 using the Bethesda criteria, and Kappa analysis showed moderate inter-rater agreement between both methods of sampling with both the BSCC and Bethesda criteria.

The finding that the anatomical spatula and cytobrush–spatula demonstrated similar results, suggests that the anatomical spatula can be used alone to prepare satisfactory cervical smear samples in most cases.

Previous reports have suggested that devices specifically designed to enhance sampling of the endocervical canal are more likely to cause cervical trauma resulting in bleeding which may, if heavy, interfere with diagnosis.[5] Our study demonstrated similar finding. 35.5% of the slides were reported to be bloody in the anatomical spatula group while 32.7% of slides from the cytobrush–spatula device were blood stained. The odds of showing absent blood staining when using the anatomical spatula is 0.89 that of the cytobrush–Ayres spatula. There was however a moderate inter-rater agreement between the two sampling devices. Fortunately, none of the blood contaminated smears in this study prohibited cytological assessment.

Conclusions

This study is limited by its relatively small sample size and its restriction to a single center, thereby making it difficult t to generalize our findings. The study however showed that cytology results from sampling with both anatomical spatula and cytobrush–spatula are similar. Even though the anatomical spatula appears to be superior in terms of cellular adequacy and adequate transformation zone sampling, there was no significant statistical difference between the two devices and there was mild to moderate inter-rater agreement in the results obtained.

It is therefore recommended that the anatomical spatula be used as collection device in conventional cytology in place of the cytobrush–spatula with the aim of improving the quality of smears without necessarily increasing the cost.

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Conflicts of interest

There are no conflicts of interest.

References

1. Albert SO, Oguntayo OA, Samaila MA. Reducing deaths from cervival cancer, examining the prevention paradigms. Obstet Gynaecol Clin North Am 2012;54:599-611.
2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108.
3. Thomas JO. Cancer registration and diagnosis in Ibadan. Arch Ibadan Med 2000;1:5-6.
4. Greening SE. The adequate Papanicolaou smear revisited. Diagn Cytopathol 1985;1:55-8.
5. Martin-Hirsch P, Jarvis G, Kitchener H, Lilford R. Collection Devices for Obtaining Cervical Cytology Samples (Cochrane Review). In: The Cochrane Library. Chichester, UK: John Wiley & Song Ltd.; 2007.
6. Martin-Hirsch P, Lilford R, Jarvis G, Kitchener HC. Efficacy of cervical-smear collection devices: A systematic review and meta-analysis. Lancet 1999;354:1763-70.
7. Blanks RG. ABC3 part II: A review of the new criteria for evaluating cervical cytology in England. Cytopathology 2012;23:360-70.
8. Giard RW. False-negative rate of cervical cytology: Sense and sensitivity. Diagn Cytopathol 2001;25:275-7.
9. van der Graaf Y, Vooijs GP. False negative rate in cervical cytology. J Clin Pathol 1987;40:438-42.
10. Aghajani Delavar M, Shafigh E, Mohamadpour RA. Comparison of cervix brush with spatula ayres for obtaining endocervical cells. J Birjand Univ Med Sci 2006;13:9-15.
11. Soleimani M, Abdali Kh, Khajehei M, Tabatabaee HR, Komar PV, Riaz Montazer N. Comparison of pap smear quality with anatomical spatula method and the common method (spatula-cytobrush): A single blind clinical trial. Iran J Cancer Prev 2012;5:33-8.
12. Paterson ME, Peel KR, Joslin CA. Cervical smear histories of 500 women with invasive cervical cancer in Yorkshire. Br Med J (Clin Res Ed) 1984;289:896-8.
13. Brink AL, du Toit JP, Deale CJ. In search of more representative cervical cytology. A preliminary prospective study. S Afr Med J 1989;76:55-7.
14. George S, Abrahams Y, Karim SZ, Kothari A. Improving the quality of cervical screening. BJOG 2004;111:960-6.
15. Martin-Hirsch P, Jarvis G, Kitchener H, Lilford R. Collection devices for obtaining cervical cytology samples. Cochrane Database Syst Rev 2000;(2):CD001036.
16. Nayar R, Wilbur DC. The Pap Test and Btehesda 2014. Cancer Cytopathol 2015;123:271-81.
17. Dahiru T, Aliyu A, Kene TS. Statistics in medical research: Misuse of sampling and sample size determination. Ann Afr Med 2006;5:158-61.
18. Al-Subaihi AA. Sample size determination. Influencing factors and calculation strategies for survey research. Saudi Med J 2003;24:323-30.
19. Buntinx F, Brouwers M. Relation between sampling device and detection

of abnormality in cervical smears: A meta-analysis of randomised and quasi-randomised studies. BMJ 1996;313:1285-90.
20. Guidance on the Use of Liquid-Based Cytology for Cervical Screening. Technology Appraisal Guidance; Published 22 October, 2003. Available from: http://nice.org.uk/guidance/tab69. [Last accessed on 2018c Apr 3].
21. Cervical cancer screening: The Pap smear. Summary of an NIH consensus statement. Br Med J 1980;281:1264-6.
22. Davey DD, Nielsen ML, Rosenstock W, Kline TS. Terminology and specimen adequacy in cervicovaginal cytology. The college of American pathologists interlaboratory comparison program experience. Arch Pathol Lab Med 1992;116:903-7.
23. Noel ML. Papanicolaou smear adequacy: The cervical cytobrush and Ayre spatula compared with the extended-tip spatula. J Am Board Fam Pract 1989;2:156-60.