

ISSN Online: 2162-2485 ISSN Print: 2162-2477

Cervical Cancer Screening, Adherence to and Challenges of Follow-Up in Resources Poor Setting

Theophilus Ogochukwu Nwankwo^{1*}, Silas Onyemaechi Okoro¹, Francis Ikechukwu Ukekwe², Leonard Ogbonna Ajah¹, Benjamin Chukwuma Ozumba¹

¹Faculty of Medical Sciences, Department of Obstetrics and Gynaecology, University of Nigeria, Nsukka, Enugu State, Nigeria ²Faculty of Medical Sciences, Department of Pathology, University of Nigeria, Nsukka, Enugu State, Nigeria Email: *theophilus.nwankwo@unn.edu.ng, *theonwankwo@gmail.com, okoroonyemaech@yahoo.com, drikukekwe@hotmail.com, Leookpanku@yahoo.com, benjamin.ozumba@unn.edu.ng

How to cite this paper: Nwankwo, T.O., Okoro, S.O., Ukekwe, F.I., Ajah, L.O. and Ozumba, B.C. (2019) Cervical Cancer Screening, Adherence to and Challenges of Follow-Up in Resources Poor Setting. *Open Journal of Preventive Medicine*, **9**, 105-114. https://doi.org/10.4236/ojpm.2019.99010

Received: July 25, 2019 Accepted: September 3, 2019 Published: September 6, 2019

Copyright © 2019 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

http://creativecommons.org/licenses/by/4.0/





Abstract

Background: Organized cervical cancer screening program has contributed to the reduction in incidence of cervical cancer in developed countries. Follow up, to ensure adherence to regular screenings, still poses challenges in poor resource settings. Objective: This study aims at determining the cervical cancer screening uptake, adherence to follow up instructions and interval cervical cancer screening and intervention to improve adherence through personalized reminders (phone calls and text messages). Methods: This was a prospective study of clients screened for cervical cancer at the University of Nigeria Teaching Hospital, Enugu from January 2012 to December 2016. The participants were studied for adherence to interval follow-up screening. Eligible participants were followed up using phone calls and text messages and the outcome noted. The data was analysed using statistical software for social sciences (SPSS) version 17. Results: The mean age and parity of 1146 participants screened for cervical intra-epithelial abnormalities within the study period was 44.18 ± 11.08 years and 3.78 ± 2.08 respectively. Most of the subjects (91.8%) screened negative to squamous intra-epithelial lesion (SIL) or malignancy, 8.2% (94/1146) had various grades of SIL. Thirty-five (37%), 29 (31%), 16 (17%) and 14 (15%) of the 94 SIL positive cases had atypical cells of unknown significance (ASCUS), low-grade squamous intra-epithelial lesion (LGSIL), high-grade squamous intra-epithelial lesion (HGSIL) and cervical carcinoma respectively. Adherence to instructions for repeat cytology was only 37.7% while that for 3 yearly interval rescreening was 17.5%. Phone calls and messages to clients improved adherence to appreciable extent. Conclusion: Adherence to interval and follow-up screening for cervical cancer was low. The use of phone calls and short message services (SMS) to remind clients

of screening appointments increased adherence and should be employed in developing countries.

Keywords

Cervical Cancer, Intra-Epithelial Lesion, Screening, Follow-Up, Adherence

1. Introduction

Cervical cancer is a major public health problem, and it is top on the list in the World Health Organization (WHO) program on Cancer Control [1]. Cervical cancer is the second most common cancer among women and the most common cause of mortality from gynaecologic malignancy worldwide [2]. In Nigeria, it is the most common gynaecological cancer as well as the most common cause of cancer death among women, with a mortality rate of 25/100,000 [3] [4]. Cancer of the cervix has a long pre-cancerous phase which makes it amenable for screening and prevention [5].

Organised Screening for neoplastic changes on the cervix has invariably contributed to the reduction of incidence of cervical cancer in developed countries [6]. Most developing countries are yet to institute organized countrywide screening [7]. Opportunistic screening has been advocated and is practiced in our institution [8].

The Papanicolaou smear was introduced by Papanicolaou in the 1930s and was endorsed by the American Cancer Society in 1945 as an important cancer-screening tool [9]. The increasing use of the Papanicolaou smear has significantly reduced the number of deaths related to cervical cancer since the 1950s. Papanicolaou smear is one component of a larger cervical cancer prevention system, which includes education, examinations, laboratory testing, and clinical procedures [10]. This system is not perfect because there is still the occurrence of morbidities and mortalities from this preventable cancer. Cervical cancer screening and treatment systems can be deficient in several ways [11].

Cancer screening is under-utilized by ethnic minorities, persons living in rural areas, the poor, the uninsured, and the elderly. Failures can result from errors in obtaining appropriate samples, inaccuracy of the test itself, incorrect interpretation of smears, and inaccurate reporting of results [9] [12]. Failures can also occur after the cervical smear results are reported. In addition, aspects of patients' biological, psychological, or social spheres can hinder or enhance their ability to adhere to the care plan communicated by their care providers [12].

Cervical cancer screening is limited or absent in several African countries including Nigeria [2]. The high mortality rate for cervical cancer in Nigerian and other developing countries may be explained by the lack of follow up to ensure adherence to instructions, even after opportunistic screening [13].

This lack of follow up may be due to a number of factors which include: shortage

of health care providers [14], lack of governmental policy on cervical cancer screening, poor attention to women's health needs especially outside maternity and family planning, poor referral systems, inequitable distribution of cervical cancer screening centers.

Currently, follow up to ensure adherence to instructions and regular interval screening for those opportunistic screening is a challenge. Previous studies to determine the rate of non-adherence to follow up for abnormal findings on Pap smear test showed variable results. The differences might be due to differences in researchers' definition of non-adherence [15].

Studies regarding cervical cancer screening have been affected by large rates of loss of patient to follow up. Overall rate of non-adherence in control population ranges from less than 10% to more than 40% [16]. An Australia study showed 64% adherence to follow up following abnormal Pap smear test [17]. Another retrospective study in the United Kingdom of over 1000 patients with abnormal pap smear test showed 59% adherence to follow up [18]. Another study in Italy showed 81% over all adherences to follow up [19]. Results from the above studies have shown that patients' non-adherence to follow up following abnormal pap smear test is a global problem that both patients and care providers share responsibility. Regular screening with cervical smear cytology every 3 years has substantial benefits than harm [20].

Miller *et al.* in a study of 828 patients with abnormal Pap smear test to evaluate the effect of use of phone calls to enhance patient adherence, found out that patient adherence was 50% without any intervention but that patient adherence increased to 68% with intervention [21]. Also Lerman *et al.* in their study of adherence to follow up in 90 women with abnormal Pap smear test, it was demonstrated that patient adherence to follow up increased from 43% without any intervention to 67% with intervention [22]. Marcus *et al.* also in a study involving 1453 women with abnormal Pap test showed an increase in adherence from 64% to 72% with intervention [23].

This study aims at determining the uptake of cervical cancer screening in our institution, adherence to follow up and intervention to improve clients' follow up through personalized reminding by phone calls and text messages.

2. Materials and Methods

Study area: Enugu is the capital of Enugu State. Enugu state is one of the five states in the South-East geopolitical zone of Nigeria. It is mainly inhabited by the Igbo speaking community and has the population of about 3,267,837 people according to 2006 population census [24]. The University of Teaching Hospital (UNTH) is a tertiary health institution located at Ituku-Ozalla, about 21 kilometres from Enugu metropolis. UNTH serves the people of old Eastern region and neighbouring northern states. Highly specialized cases are also referred from as far as Cameroun. The hospital has a well-developed Obstetrics and Gynaecology Department with an established cancer screening centre.

Study design: This was a cross-sectional descriptive study of clients that received cervical cancer screening in the University of Nigeria Teaching Hospital, Enugu within a 5 year period from January 2012 to December 2016. The study participants were consenting women who attended the cervical cancer screening Clinic, UNTH. The women were counselled on cancer of the cervix, the screening procedures, and objectives of the study, following which, consent to participate in the study was sought and obtained.

The Pap smear cytology result was reported using the Bethesda 2001 system [25]. For the purpose of this study; the Pap smear cytology result was negative when it was negative for intra-epithelial lesion or malignancy but positive when there was cervical epithelial abnormality.

Those that were due for interval follow-up screening and those instructed for various reasons to repeat screening were identified, counselled and studied for adherence. These groups were called on their submitted phone numbers for one and one discussion inquiring about their interval follow up screening and reminding them to do so if they had not. Short Message Service (SMS) bearing the same messages were sent to those that didn't respond to phone calls. Those that answer the phone calls and interacted with the researcher or replied the SMS messages sent to their phone numbers are identified as positive phone response while those who did not answer their phone calls or failed to respond to SMS messages were recorded as negative response. Those that presented for repeat screening within 6 months were also recorded.

Exclusion criteria comprised women who were less than 20 years, pregnant women and those within 6 weeks post-partum as well as the women who, despite adequate counselling, declined to participate in the study.

The clients' demographic characteristics and results of their cervical cancer screening were extracted from their hospital records. The data was processed and analysed using frequencies, mean and descriptive statistics by software for SPSS version 17 (SPSS Inc., Chicago, IL, USA). The level of significance was set at ≤ 0.05 .

The ethical clearance for this study was obtained from the Health Research Ethics Committee of UNTH.

3. Results

One thousand one hundred and forty six participants were primarily screened within the period and had received their results. One hundred and thirty five were asked to repeat screening within 6 months for various reasons.

Table 1 shows the demographic characteristics of the participants. Their mean age was 44.18 ± 11.08 years with a range of 20 - 66 years. Their mean parity was 3.78 ± 2.08 with a range of 1 - 8. Majority (85.78% (983/1146)) were married while only 13.70% (157/1146) were single. While 13.7% (157/1146) of the participants were unemployed, the rest were employed with civil and public servants predominating. A total of 65.53% (751/1146) were urban dwellers while 34.47% (395/1146) were rural dwellers. Also 59.6% (683/1146) were referred

from gynaecological clinic, while 40.4% (463/1146) came on their own accord. Most of the subjects, 91.8% (1052/1146) screened negative to cervical squamous intraepithelial lesion or malignancy, 12.07% (127/1052) of those that screened negative however had inflammatory cells suggestive of cervicitis. 8.2% (94/1146) had various grade of cervical intra-epithelial lesions.

Figure 1 shows a pie chart of the percentages of abnormal cervical screening results. Of the 94 that had abnormal cytology reports of cervical lesion, 37% (35/94) had atypical cell of unknown significance (ASCUS), 31% (29/94) had low grade squamous intraepithelial lesion, 17% (16/94) had high grade squamous intraepithelial lesion. 15% (14/94) had cervical carcinoma.

Follow up: **Figure 2** shows the bar chart of responses to phone call and, interval/ reschedule Screening, 37.78% of 135 instructed to repeat cervical screening, complied and their results were all normal while 62.2% (84/135) defaulted. Of the 1146 screened within this period, 565 (49.30%) were due for 3 yearly interval rescreening out of which only 99 (17.52%) had rescreened and were normal. More than 99% (1135/1146) had their phone number registered with the hospital, however only 55.15% (632/1146) responded to phone calls and SMS messages sent to them. Only 7.94% (37/466) of women had presented to hospital for rescreening within 6 months of phone interaction. The 14 cases of invasive cancer of the cervix diagnosed during the screening had colposcopic evaluation that confirmed lesion and they were offered extended hysterectomy, 8 of them had presented for vault smear screening which were normal. Those that had LGSIL and HGSIL were sent for colposcopic evaluation which they complied.

4. Discussion

The main focus of this study is on fidelity to follow up among women screened for cervical cancer and intervention to improve adherence to follow up instructions. It may be pertinent however to comment on the low prevalence of SIL found in this study. This prevalence of 8.2% is the lowest reported in institutions in our environment, in contrast to higher prevalence of 29.3% and 22.07% reported by other researchers in Nnewi in South eastern and Ife in Southern western parts of Nigeria respectively [2] [3]. Some other earlier studies in various regions of Nigeria, reported closer but slightly higher prevalence ranging from 11% to 13% [1] [5] [26] [27]. The low prevalence found in this study may indicate decreasing prevalence of SIL in our environment. Further studies however are needed to elucidate this trend. The finding in this study of 1146 women screened for cervical cancer over 5 years in our institution suggests improvement in cervical cancer screening up take. This is in contrast to the report by Chukwuani et al. and Obi et al. of less than a thousand cervical cancer screenings over 10 years in their studied institutions in the same environment [26] [27]. Cervical epithelial abnormalities were significantly more common among women who were 40 years and above, and single/separated women as well as widows (P-value ≤ 0.05).

This study further reported that 15% of 94 women who had abnormal Pap

smear cytology already had micro-invasive cancer. This is higher than 14 (1.4% of overall screening) reported by previous study in our environment [27]. This persisting discovery of micro-invasive cervical cancer during Pap smear cytology in our institution may be attributable to lack of organized screening program in our nation. Concerned individuals, stake holders and academics should continue to champion opportunistic screening in poor resource countries while advocating for establishment of organized cervical cancer screening in these settings.

Follow up and adherence to instructions in cervical cancer screening is a challenge even in developed counties. The high mortality rate for cervical cancer in Nigerian and other developing countries may be explained by lack of follow up to ensure adherence to instructions, even after opportunistic screening. This study

Table 1. Demographic characteristics of subjects.

Characteristics	Mean in Years	Standard Deviation
Age	44.18	11.8
Parity	3.78	2.08
	Frequency	Percentage
Marital Status		
1) Single	157	13.70
2) Married	983	85.78
3) Divorced/Separated	4	0.35
4) Widowed	2	0.17
Dwelling Place		
1) Urban	751	65.53
2) Rural	395	34.47
Employment Status		
1) Formal sector employed	562	49.04
2) Self Employed	427	37.26
3) Unemployed	157	13.70
Sources of Referral		
1) Within the facility	988	86.21
2) Private facilities	125	10.91
3) Self referred	33	2.88

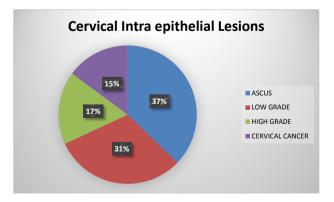


Figure 1. Pie Chart showing the percentage distribution of cervical intra-epithelial lesions.

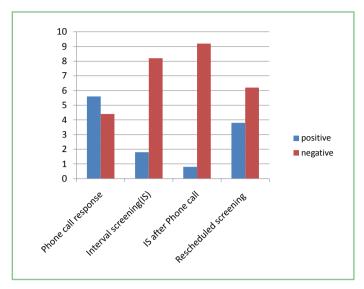


Figure 2. Bar Chart showing responses to phone call and, interval/reschedule screening.

found an adherence rate of 37.78% and hence 62.22% loss to follow up among those that had abnormal cervical cytology in their initial screening and were requested to repeat the screening after 6 months. It also reported an adherence rate of 17.52% and 82.48% loss to follow up among those were due for 3 yearly interval rescreening. Chukwuani and Obi et al. reported in their studies that only 0.4% and 1.4% had history of previous cervical cancer screening [26] [27]. Marcus et al. in their study in United States of America (USA) reported 29% overall loss to follow up (i.e. 71% adherence rate) [23]. Studies in other developed countries such as United Kingdom, Australia and Italy reported quite higher adherence rate of 59%, 64% and 81% respectively than the finding in this study [17] [18] [19]. The finding in this study collaborates that of other studies this suggests that patients' loss to follow among those screened for SIL is a global challenge. The disparities in the findings of this study and others from developed counties may be due to prevalent health Policy, government commitment and other Patients and care givers demographics. Patients and their care giver share in this responsibility. Ineffective communication of results and recommendations by care providers is an important factor in patients' loss to follow up.

Some specific interventions have been reported by various studies to enhance fidelity to follow up among women screened for SIL. Yabroff *et al.* in their meta-analyses of studies on interventions designed to enhance follow up of patients with abnormal Pap smear, reported that interactive phone call counseling was most effective, and improved adherence by 24% - 31%. Patient reminding also improved follow up adherence by 18% [28]. Miller *et al.* in a study of 828 patients with abnormal Pap smear test to evaluate the effect of use of phone calls to enhance patient adherence, found out that patient adherence to follow up was enhanced from 50% without to 68% by phone call intervention. Individuals that received telephone counseling were significantly more likely to adhere to follow

up than those that just received telephone confirmation of result [21]. Lerman *et al.* in their study of adherence to follow up in 90 women with abnormal pap smear test, also reported that patient adherence to follow up was increased from 43% to 67% by telephone intervention [22]. Marcus *et al.* also in a study involving 1453 women with abnormal Pap test showed that adherence to follow up was increased from 64% to 72% by telephone intervention [23].

More than 99% of the participants in this study had their phone number registered with the hospital, however only 55.15% (632/1146) responded to phone calls and SMS messages sent to them, this underscore the need to employ other methods of interventions such as transportation assistant, Education pamphlets, home visiting or use of explanatory brochure to improve patient adherence to follow up. However, these methods of intervention pose a big challenge in poor resource setting like ours.

This study showed that only additional 7.94% of the patients came for follow among those that had abnormal Pap smear who were asked to rescreen after six month following intervention by phone call/SMS message. This thus increased the level of adherence rate from 37.78% to 45.72%.

5. Conclusion

There was encouraging uptake of cervical cancer screening in our institution. Adherence to interval and follow up screening was however very low. Current technology that would enhance follow-up is available and is at the reach of these clients. Automated phone calls or SMS reminding subjects of the screening appointment should be employed to improve adherence.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Ajah, L.O., Ezeonu, Iyoke, C.A., Nkwo, P.O. and Ajah, M.I. (2015) A Five Year Review of Cervical Cytology in Abakaliki, Nigeria. *American Journal of Cancer Prevention*, **3**, 23-26.
- [2] Akinfolarin, A.C., Olusegun, A.K., Omoladun, O., Omoniyi-Esan, G.O. and Onwundiegu, U. (2017) Age and Pattern of Pap Smear Abnormalities: Implications for Cervical Cancer Control in a Developing Country. *Journal of Cytology*, 34, 208-211. https://doi.org/10.4103/JOC.JOC_199_15
- [3] Mbamara, S.U., Ukah, C.O., Onyiaorah, C.I., Ikpeze, O. and Okonkwo, J. (2014) The Pattern of Cervical Cytology in Women Attending Various Clinics at a Tertiary Hospital in Anambra Southeast, Nigeria. *British Journal of Medicine and Medical Research*, 4, 5218-5228. https://doi.org/10.9734/BJMMR/2014/11345
- [4] Lee, J.K., So, K.A., Piyathilake, C.J. and Kim, M.K. (2013) Mild Obesity, Physical Activity, Calorie Intake, and the Risks of Cervical Intraepithelial Neoplasia and Cervical Cancer. *PLoS ONE*, 8, e66555. https://doi.org/10.1371/journal.pone.0066555

- [5] Nnadi, D.C., Nwobodo, E.L., Ekele, B.A. and Sahabi, S.M. (2014) Screening for Cervical Cancer: A Review of Outcome among Infertile Women in a Tertiary Hospital in North-West Nigeria. *Annals of Medical and Health Science Research*, 4, 383-387. https://doi.org/10.4103/2141-9248.133464
- [6] American Society for Colposcopy and Cervical Pathology (ASCCP) (2015) Screening Guidelines 2015.
- [7] World Health Organization (2007) The WHO Strategic Approach to Strengthening Sexual and Reproductive Health Policies and Programmes. WHO, Geneva.
- [8] Onah, H.E., Ezugwu, F.O. and Eze, J.N. (2001) Cervical Cancer Screening: A Survey of Current Practice amongst Nigeria Gynaecologists. *Tropical Journal of Obstetrics* and Gynaecology, 18, 78-81. https://doi.org/10.4314/tjog.v18i2.14435
- [9] Lieu, D. (1996) The Papanicolaou Smear: Its Value and Limitations. *The Journal of Family Practice*, **42**, 391-399.
- [10] Koss, L.G. (1989) The Papanicolaou Test for Cervical Cancer Detection. A Triumph and a Tragedy. *JAMA*, **261**, 737-743. https://doi.org/10.1001/jama.261.5.737
- [11] Koss, L. (1993) Cervical (Pap) Smear. New Directions. *Cancer*, **71**, 1406-1412. https://doi.org/10.1002/cncr.2820710405
- [12] National Cancer Institute Cancer Screening Consortium for Underserved Women (1995) Breast and Cervical Cancer Screening among Underserved Women. Baseline Survey Results from Six States. Archives of Family Medicine, 4, 617-624. https://doi.org/10.1001/archfami.4.7.617
- [13] Nene, B.M., Deshpande, S., Jayant, K., Budukh, A.M., Dale, P.S., et al. (1996) Early 168 Detection of Cervical Cancer by Visual Inspection: A Population-Based Study in Rural India. *International Journal of Cancer*, 68, 770-773. https://doi.org/10.1002/(SICI)1097-0215(19961211)68:6<770::AID-IJC14>3.0.CO;2-4
- [14] Dim, C.C., Ezegwui, H.U., Ikeme, A.C., Nwagha, U.I. and Onyedum, C.C. (2011) Prevalence of Cervical Squamous Intraepithelial Lesions among HIV-Positive Women in Enugu, South-Eastern Nigeria. *Journal of Obstetrics and Gynaecology*, 31, 759-762. https://doi.org/10.3109/01443615.2011.598967
- [15] Khanna, N. and Phillips, M.D. (2001) Adherence to Care Plan I Women with Abnormal Papanicolaou Smears: A Review of Barriers and Interventions. *The Journal of the American Board of Family Practice*, **14**, 123-130.
- [16] Schofield, M.J., Sanson-Fisher, R., Halpin, S. and Redman, S. (1994) Notification and Follow-Up of Pap Test Results: Current Practice and Women's Preferences. *Preventive Medicine*, **23**, 276-283. https://doi.org/10.1006/pmed.1994.1039
- [17] Mitchell, H. and Medley, G. (1989) Adherence to Recommendations for Early Repeat Cervical Smear Tests. *BMJ*, 298, 1605-1607. https://doi.org/10.1136/bmj.298.6688.1605
- [18] Elwood, J.M., Cotton, R.E., Johnson, J., Jones, G.M., Curnow, J. and Beaver, M.W. (1984) Are Patients with Abnormal Cervical Smears Adequately Managed? *British Medical Journal (Clinical Research ed.)*, 289, 891-894. https://doi.org/10.1136/bmj.289.6449.891
- [19] Ronco, G., Iossa, A., Naldoni, C., et al. (1998) A First Survey of Organized Cervical Cancer Screening Programs in Italy. GISCi Working Group on Organization and Evaluation. Gruppo Italiano Screening Citologico. *Tumori*, 84, 624-630. https://doi.org/10.1177/030089169808400602
- [20] Agency for Healthcare Research and Quality (2014) Screening for Cervical Cancer. In: *Guide to Clinical Preventive Services. Report of the US Preventive Services Task Force*, 34. https://www.uspreventiveservicestaskforce.org/

- [21] Miller, S.M., Siejak, K.K., Schroeder, C.M., Lerman, C., Hernandez, E. and Helm, C.W. (1997) Enhancing Adherence Following Abnormal Pap Smears among Low-Income Minority Women: A Preventive Telephone Counseling Strategy. *Journal of the National Cancer Institute*, 89, 703-708. https://doi.org/10.1093/jnci/89.10.703
- [22] Lerman, C., Hanjani, P., Caputo, C., *et al.* (1992) Telephone Counseling Improves Adherence to Colposcopy among Lower-Income Minority Women. *Journal of Clinical Oncology*, **10**, 330-333. https://doi.org/10.1200/JCO.1992.10.2.330
- [23] Marcus, A.C., Kaplan, C.P., Crane, L.A., et al. (1998) Reducing Loss-to-Follow-Up among Women with Abnormal Pap Smears. Results from a Randomized Trial Testing an Intensive Follow-Up Protocol and Economic Incentives. Medical Care, 36, 397-410. https://doi.org/10.1097/00005650-199803000-00015
- [24] Enugu State of Nigeria. https://www.britannica.com/place/Enugu-state-Nigeria
- [25] Solomon, D., Davey, D., Kurman, R., Moriarty, A., O'Connor, D., Prey, M., et al. (2002) The 2001 Bethesda System Terminology for Reporting Results of Cervical Cytology. JAMA, 287, 2114-2119. https://doi.org/10.1001/jama.287.16.2114
- [26] Chukwuani, L.I., Onuigbo, W.I.B. and Mgbor, N.C. (2003) Cervical Cancer Screening in Enugu, Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, 20, 109-112. https://doi.org/10.4314/tjog.v20i2.14412
- [27] Obi, A.N., Ozumba, B.C., Nwokocha, A.R. and Waboso, P.A. (2007) Participation in Highly Subsidised Cervical Cancer Screening by Women in Enugu South-East Nigeria. *Journal of Obstetrics and Gynaecology*, 27, 305-307. https://doi.org/10.1080/01443610701227976
- [28] Yabroff, K.R., Keener, I.F. and Mandelbratt, J.S. (2000) Effectiveness of Interventions to Improve Follow-Up after Abnormal Cervical Screening. *Preventive Medicine*, **31**, 429-439. https://doi.org/10.1006/pmed.2000.0722