East African Medical Journal Vol. 97 No. 10 October 2020
TRIAGING WOMEN WITH POSITIVE VISUAL INSPECTION WITH ACETIC ACID (VIA) RESULTS WITH LIQUID BASED CYTOLOGY (LBC) AT CIMAS MEDICAL LABORATORIES, ZIMBABWE
Raymond Chibvongodze (HBMLS, MSc Clinical Cytology, MSc Histopathology), Lecturer, Department of Medical Laboratory Sciences, University of Zimbabwe, P.O. Box A178, Avondale, Harare, Zimbabwe, Tafadzwa Dupwa, (HBMLS, MSc QMS), Medical Laboratory Scientist, Clinical Trial Research Centre. University of Zimbabwe P.O. Box A178, Avondale, Harare, Zimbabwe, Lucy Wangari Muchiri (PhD Clinical Cytology, MMED Pathology, MBChB), Associate Professor, Department of Human Pathology, Unversity of Nairobi, P.O. Box 30197 – 00100, Nairobi, Kenya.

Corresponding author: Raymond Chibvongodze,,Department of Medical Laboratory Sciences, University of Zimbabwe P.O. Box A178, Avondale, Harare, Zimbabwe, Email: rayscientist@gmail.com.

TRIAGING WOMEN WITH POSITIVE VISUAL INSPECTION WITH ACETIC ACID (VIA) RESULTS WITH LIQUID BASED CYTOLOGY (LBC) AT CIMAS MEDICAL LABORATORIES, ZIMBABWE

R. Chibvongodze, T. Dupwa, L.W. Muchiri

ABSTRACT

***Background*: Visual Inspection with Acetic Acid (VIA) has a low specificity for the detection of cervical lesions. It is therefore, necessary to subject those found positive to cytological assessment so as to avoid referrals for cryotherapy.**

***Objectives*: To determine Liquid Based Cytological (LBC) findings in VIA positive women and also estimate the proportion of women who could be spared from cryotherapy.**

***Materials and Methods*: This study was a cross sectional descriptive study. Consecutive sampling method was used. A Thin Prep 2000 machine was used to process the LBC samples which were then stained using the Papanicolaou stain. The 2014 Bethesda System was used to report the LBC smears.**

***Results*: Of the 205 VIA positive women enrolled in the study, 6 (2.9%) had an unsatisfactory interpretation, 145 (70.7%) had an NILM interpretation, 27 (13.2%) had an ASCUS interpretation, 7 (3.4%) had an LSIL diagnosis, 2 (1.0%) had an ASC-H interpretation and 18 (8.8%) had a HSIL diagnosis. Of the 145 NILM cases, 35 (24%) were reported as inflammatory, 2 (1.4%) had *Candida* infections and 5 (3.4%) had Bacterial vaginosis.**

***Conclusion*: Most (70.7%) VIA positive women had no cytological detectable lesions and therefore were requested for follow up as per protocol. This study recommends subjecting all who are VIA positive to have a cytological test and follow up.**

INTRODUCTION

Cervical cancer is the third most common malignancy in women worldwide.[1] However, in Zimbabwe, it is the most common malignancy regardless of gender contributing 35% of all diagnosed cancers.[2] Cervical cancer is the leading cause of mortality in Zimbabwe.[3] This is attributed to non-availability of mass cervical cancer screening programs.[4]

Cervical cancer neoplasia is slow growing, taking several years to decades from HPV infection to a histologically detectable lesion.[5] This enables interventions possible before a precancerous cervical lesion becomes an invasive cancer. The interventions include screening to detect and treat the premalignant lesions.[6] Prevention of invasive cervical cancer is important because treatment resources for invasive cervical cancer are scarce and expensive in Zimbabwe. Parkin et al documented a cervical cancer survival rate of 21% in Africa compared to 70% in United States of America.[7] This difference can be due to late presentation of patients with advanced disease to healthcare centers in Africa.[8]

Cervical cancer has remained a major cause of mortality in developing countries because Pap smear-based screening programs have major barriers such as serious shortage of trained Cytologists and poor health infrastructure.[9] In addition, cytology is not a point of care tests as they require patients with abnormal cytology to be notified to come for treatment. This introduces another barrier of high loss to follow up.[10] Cronje et al recorded a defaulter rate of >60% in African countries.[11] Collectively, these barriers result in patients presenting late and with advanced diseases to health facilities.

In view of these barriers, alternative methods of screening for cervical precancerous lesions were developed and recommended for low resource countries.[9] Screening programs based on VIA enhanced accessibility to cervical cancer screening and treatment by cryotherapy, the 'Single Visit Approach'.[9] A negative VIA result rules out the existence of a serious cervical lesion as evidenced by their NPV of 99%[12]. The limitations of VIA include high subjectivity and non-specificity because false positive results can occur due to other non-neoplastic conditions such as cervicitis.[9] This is supported by Sritipsukho et al who recorded a low PPV of 17%.[12]

All cervical cancer screening methods currently in use in Zimbabwe: Pap smears, VIA, and HPV DNA testing (in a few settings) have their limitations[16]. According to WHO management guidelines, patients who tests VIA positive should either be treated by cryotherapy or further evaluated by using colposcopy.[9] However, the treatment of all positive cases may result in overtreatment of disease-free patients and wastage of scarce treatment resources. Referring all VIA positive cases on the other hand, overwhelms the referral health centers and this complicates the accessibility of screening and treatment services in Zimbabwe.

In response to this, other centers in Zimbabwe use LBC to triage VIA positive patients. The LBC is used to identify cases for referral for colposcopy. This approach would minimize unnecessary treatment in disease free women while reducing the number of women referred for colposcopy. This study, therefore, aimed at determining LBC findings in VIA positive women and estimating of the proportion of women who were spared from unnecessary cryotherapy treatment at Cimas Medical Services.

MATERIALS AND METHODS

Study design

This study was a cross-sectional descriptive study from January 2017 to March 2020.

Sampling method

Consecutive sampling method was used in this study for the cases that fulfilled the study entry criteria. Only women with positive VIA results were enrolled in this study.

Study objectives

To determine Liquid Based Cytological (LBC) findings in VIA positive women and to estimate the proportion of women who could be spared from unnecessary cryotherapy treatment by triaging VIA positive women with LBC at Cimas Medical Services.

Study population and sample size

A total of 3372 women were screened for cervical cancer using VIA during the study period. Only 205 women (6.1%) had VIA positive results and were enrolled into this study. Patients with a positive VIA result had an LBC sample collected on the same visit.

Liquid Based Cytology smears preparation

A Thin Prep 2000 machine (Hologic Inc – Marlborough, MA 01752, USA) was used to deposit a monolayer of cells on to a Thin Prep charged microscopy slides (Hologic Inc – Marlborough, MA 01752 USA). The LBC slides were stained using the Papanicolaou stain.

LBC slides interpretation

The slides were reported using the 2014 Bethesda System of reporting cervical smears. The LBC smears were evaluated by the principal investigator, a Clinical cytologist (MSc, Clinical Cytology) and a pathologist (MMED, Anatomic Pathology) for the presence or absence of epithelial abnormality. Discrepant findings were referred to a third person, a pathologist (MMED Anatomic Pathology). The third pathologist was blinded of the results of the first two reviewers.

Data Management

Patients eligible for the study (VIA positive women) were assigned a unique study number and the following data was captured: age, date of last menstrual period and any clinical symptoms noted during clinical examination. After evaluation of the LBC samples, the LBC results and all prior data were stored in an IBM SPSS software version 21. Information stored in soft copies was protected from access from unauthorized persons by a password which was changed periodically. The data was analyzed used the IBM SPSS software version 21. Descriptive statistics were presented as proportions, tables and charts.

Ethical Approval

Ethical approval was obtained from Joint University of University and Parirenyatwa Hospital Ethical Review Committee (JREC), certificate number: 15/2019. Permission was also granted by Cimas Medical Services for access to the data. During the study, strict patient confidentiality was observed.

RESULTS

VIA results of patients screened for cervical cancer during the study period.

Of the 3372 patients screened for cervical cancer, 205 (6.1%) had VIA positive results, 18 (0.5%) had suspicious VIA results and 3149 (93.4%) had VIA negative results. Patients with suspicious and positive VIA results had an LBC sample taken for evaluation.

Age distribution

A total of 205 study participants with a prior history of VIA positive results were recruited into the study. The mean (SD) age of the study participants was 40.4 (8.3) years and the range as 18-75 years. Figure 1 below shows

the age distribution of the study participants with a peak in the age group 30-40 years.

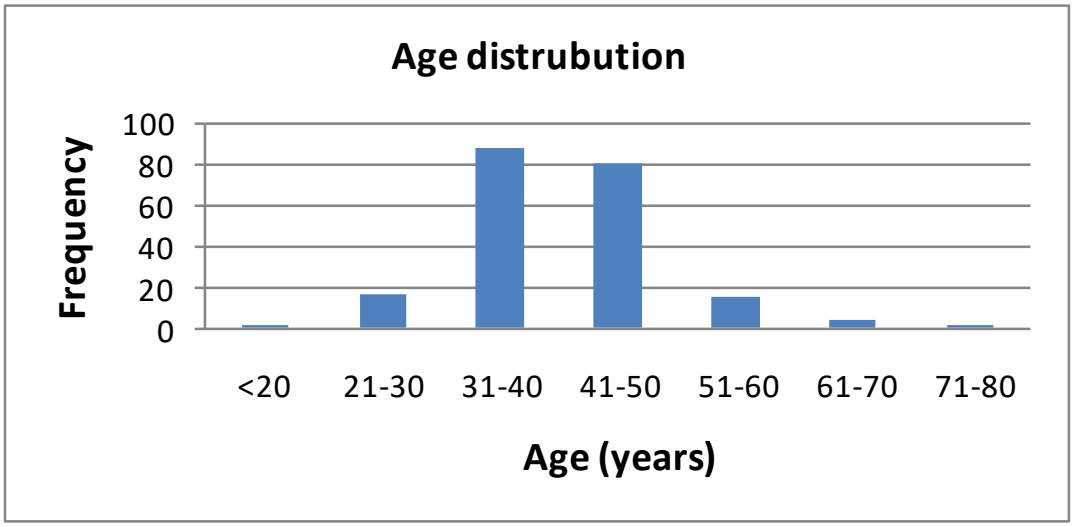

Figure 1: Age range and distribution of the study participants.

LBC results of women with positive VIA results.

Of the 205 cases, 6 cases (2.9%) had an unsatisfactory interpretation, 145 cases (70.7%) had an NILM interpretation, 27 cases (13.2%) had an ASCUS interpretation, 7 cases (3.4%) had an LSIL diagnosis, 2 cases (1.0%) had an ASC-H interpretation and 18 cases (8.8%) had a HSIL diagnosis. The studied 145 NILM cases; 35 (24%) were reported as inflammatory, 2 (1.4%) had *Candida i*nfections and 5 (3.4%) had Bacterial vaginosis.

An estimate of women who were spared from unnecessary cryotherapy.

Triaging VIA positive women with LBC reduced overtreatment by cryotherapy in 70% of VIA positive women at Cimas Medical Services.

DISCUSSION

Visual inspection with acetic acid (VIA) is the most popular cervical cancer screening method in Zimbabwe because of its single visit approach (SVA) where patients are screened and treated by cryotherapy on the same visit.[9] However, VIA is well known for having numerous false positive results due to non-neoplastic conditions such as cervicitis.[13] This study, therefore, aimed at investigating the LBC findings in VIA positive women as well as to give an estimate the proportion of women who could be spared from unnecessary cryotherapy treatments.

Study participants had a mean age of 40.4 years and this is comparable to the mean age of 38.6 years reported by Jeronino et al.[6] WHO prohibits the use of VIA for screening women above 50 years.[18] This is because the transformation zone recedes into the endocervical canal and makes it difficult to visualize it.[18] In this study 10.1% of women were above 50 years. This shows a gap in appreciating relevant knowledge in this subject in some service providers. Pap smear and HPV testing is recommended in this group of women.[19] There is need for continuous education to healthcare providers so that ethical rights of women in this age group are not violated.

The Bethesda system of reporting cervical smears recommends patients with ASCUS and LSIL results to be followed up by repeated testing after 6 and 12 months respectively while those with ASC-H and

HSIL are recommended for colposcopy.[19] Therefore, only 20 (9.8%) (HSIL and ASC-H categories) were recommended for colposcopy and 34 (16.6 %) (ASCUS and LSIL categories) were recommended for a repeat Pap smear after 6-12 months. Therefore 145 (70.7%) (NILM cases) were spared from unnecessary cryotherapy treatment by triaging VIA positive women with a Pap smear. This went far in saving the scarce treatment resources for more deserving cases.

Mabeya et al reported a cervical lesion (≥ ASCUS) detection rate of 44% in VIA+/HIV+ patients.[20] This is significantly higher than the 9.8 % in this study. This may be explained by the fact that only HIV infected patients were enrolled in that study unlike ours that did not look at HIV status for inclusion or exclusion of study participants. HIV infected patients are known to be more susceptible to having cervical lesions than HIV negative patients due to immunosuppresion.[9]

Infections and non-specific inflammation were documented as major causes of positive VIA results.[9] The detection rate of infections in this study was 3.5% which is lower than the detection rate of 6.5% recorded by Lewis et al.[21] However, the sensitivity of Pap smear in the detection of infections is low as recorded by Avwioro O *et al* which had a sensitivity of 25.25% for the detection of fungal infections.[21] Avwioro O *et al* reported that the sensitivity of the Pap smear was poor in the detection of mild Candida infections.[21]The low sensitivity of the Pap smear in the detection of infections may have contributed to a higher rate of nonspecific inflammation (19.1%) in this study.

VIA is reported to have a high sensitivity of 97% and a low specificity of 36%.[9] The small number of abnormal cytology results in VIA+ may therefore be explained by the low specificity of VIA. About 3% of the LBC samples had unsatisfactory results. This limited us from determining the presence or absence of epithelial abnormality in such patients.

CONCLUSION

Most (70.7%) VIA positive women had no cytological detectable lesions and therefore were requested for follow up as per protocol. This study recommends subjecting all who are VIA positive to have a cytological test and follow up.

REFERENCES

1. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Available from: *http://doi.org/10.3322/caac.21492.* Accessed on 15.12.18

2. National cancer prevention and control strategy for Country B: 2013-17. Available from: *https://www.iccpportal.org/sites/default/files/plans/CANCER%20STRATEGY%20FINAL%202013%202017.pdf.*Accessed on 25.02.19.

3. Yang BH, Bray FI, Parkin DM et al. Cervical cancer as a priority for prevention in different world regions: an evaluation using years of life lost. Int J Cancer. 2008,109 (3): 418-24.

4. Parkin D, Ferlay J, Hamdi-Cherif M et al. Cancer in Africa: Epidermiology and Prevention. IARC Sci Publ. 2003;153: 1-414.

5. Mitra A, MacIntyre DA, Marchesi JR et al. The vaginal microbiota, human papillomavirus infection and cervical intraepithelial neoplasia: what do we know and where are we going next? Microbiome. 2016;4:58.

6. Jeronimo J, Morales O, Horna J, Pariona J, Manrique J, Rubiños J et al. Visual inspection with acetic acid for cervical cancer screening outside of low-resource settings. Rev Panam Salud Publica. 2005;17(1):1–5.

7. Parkin DM, Bray F, Ferlay J et al. Global Cancer Statistics, 2002. A Cancer J Clin. 2005;55(2):74–108.

8. Asharaf H. Poor nations need more help to slow growing cancer burden: the International Atomic Energy Agency asks donors to provide millions of dollars to buy radiotherapy equipment. Lancet. 2003;361(9376):2209.
9. Anderson J, Lu E, Sanghvi H et al. Cervical Cancer Screening and Prevention for HIV-Infected Women in the Developing World. Cancer prevention- from mechanisms to transitional benefits. 2012. p. 231–4. Available from *www.intechopen.com.* Accessed on 12.03.19
10. Anorlu RI. Cervical cancer: the sub-Saharan African perspective. Reprod Heal Matters. 2008;16(32):41–9.
11. Cronje H. Screening for cervical cancer in developing countries. Int J Gynaecol Obs. 2004;84(2):101–8.
12. Sritipsukho P, Thaweekul Y. Accuracy of visual inspection with acetic acid (VIA) for cervical cancer screening: a systematic review. J Med Assoc Thai. 2010;97(3).
13. Gage JC, Rodriguez AC, Jeronimo J . An Evaluation by Midwives and Gynecologists of Treatability of Cervical Lesions by Cryotherapy Among Human Papillomavirus– Positive Women. Int J Gynecol Cancer. 2009;19(4):728–33.
14. Cremer M, Conlisk E, Maza et al. Adequacy of Visual Inspection with Acetic Acid in Women of Advancing Age. Int J Gynaecol Obs. 2011;113(1):68–71.
15. Zhao FH, Lin MJ, Chen F et al. Performance of high-risk human papillovirus DNA testing as a primary screen for cervical cancer: a pooled analysis of individual patient data from 17 population-based studies in China. Lancet Oncol. 2010;11(12):1160–71.
16. Eftekhar Z, Rahimi-Moghaddam P, Yarandi F et al. Accuracy of Visual Inspection with Acetic Acid (VIA) for Early Detection of Cervical Dysplasia in Tehran, Iran. Asian Pacific J Cancer Prev. 2005;6:69–71.
17. Shastri S, Dinshaw K, Amin G et al. Concurrent evaluation of visual, cytologic and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai India. Bull World Heal Organ. 2005;83:186–94.
18. World Health Organisation. Comprehensive cervical cancer control: a guide to essential practice. Switzerland: WHO Press; 2006. Available at: *http://whqlibdoc.who.int/publications/2006/9241547006_eng.pdf.* Accessed on May 5, 2019.
19. Wilbur DC, Nayar R. The Bethesda System for Reporting Cervical Cytology: Definations, Criteriaand Explanatory notes. 3rd ed. Springer. 2015 : 89-109.
20. Mabeya H, Khozaim K, Liu T et al. Comparison of Conventional Pap Smear and Visual Inspection with Acetic Acid (VIA) in HIV- Infected Women in Western Kenya. J Low Genit TractDis. 2012 ;16(2):92-7.
21. Avwioro O, Olabiyi O. Sensitivity of a Papanicolaou smear in the diagnosis of candida albicans infection of the cervix. N Am J Med Sci. 2010, 2(2):97-99.