ISSN 2282-0930 • Epidemiology Biostatistics and Public Health - XIII[th] SISMEC Congress - Vol. 20 Suppl. 1

Prevention of Cervical Cancer in a Rural Primary Care Centre in Eswatini

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BACKGROUND

Cervical cancer is a priority public health concern in the Kingdom of Eswatini, primarily due to a high incidence rate of high-risk human papillomavirus (HR-HPV) infection [1,2]. Socio-cultural, economic, and policy-related barriers often limit women's access to essential screening and preventive services, resulting in delayed diagnoses and high mortality rates [3]. Test invasiveness and sampling modalities may further reduce women's participation in existing screening programs implemented mainly through Visual Inspection with Acetic Acid (VIA), [4, 5, 6, 7].

Since May 2023, the 4-valent (4v, HPV-6, 11, 16, 18) HPV vaccine has been offered to girls aged 9–14, with an estimated 79% of the target population vaccinated by May 2025 [8,9,10]. However, data on the prevalence and genotype distribution of HPV in Eswatini are limited, and prevention strategies do not rely on local epidemiological data that are currently missing.

OBJECTIVES

In line with WHO recommendations for HPV-DNA testing as a primary screening method, this project aims to identify and address implementation challenges by implementing a "screen, triage, and treat" prevention programme featuring non-invasive urine-based HR-HPV testing at St. Philip's Clinic, a rural primary care centre in the Lubombo region of Eswatini. Specific objectives are to assess feasibility, acceptability, effectiveness, and cost-effectiveness of urine-based HR-HPV testing with the aim to enhance access among adolescent girls and women (AGW). Furthermore, it aims to evaluate the distribution of HPV genotypes in this area of Eswatini.

METHODS

A 12-month cross-sectional pilot study (February 2023–February 2024) was conducted at St. Philip's Clinic, Eswatini. Women aged 12-49 presenting for any reason were asked to provide a 30 mL urine sample. A 10 mL aliquot was centrifuged to concentrate viral particles and eliminate debris, and the Xpert® HPV test was performed locally to detect 14 high-risk HPV (HR-HPV) genotypes. Women aged 21-49 were additionally offered cervical brush testing for cytological analysis to be performed at Mbabane Central Pathology Laboratory. Screening-positive women underwent VIA to establish the need for local treatment or hospital referral according to the national screening programme. Concentrated urine samples were also dried on filter paper (dried urine spots, DUS) and sent to Italy for comprehensive HPV genotyping using in-house PCR, sequencing, and Ampliquality HPV-Type Express assay.

RESULTS

The study enrolled 510 AGWs (median age 29). 37% (190/510) were HIV-positive. First-time screenings accounted for 45% of women (228/510). The Xpert® HPV test provided valid results for 473 participants (93%), detecting HR-HPV in 42% (199/473). Women aged 21–25 had the highest HR-

DOI: 10.54103/2282-0930/29181

HPV prevalence (55%, 56/101). HIV-positive participants had a 1.8-fold increased risk of HR-HPV infection compared with the HIV-negative (95%CI 1.23–2.64). Cervical brush samples were collected for 220 women consecutively recruited from the start of the project and high-grade lesions were identified in 46 women, with 7 cases of CC, including 2 in women under 30.

Overall, 333 DUS were successfully genotyped in Italy. HPV35 was the most frequently identified genotype (24%, 80/333), followed by HPV16 (18%, 61/333), and the predominant genotype among high-grade lesions (33%, 15/46) and the sole oncogenic genotype in 15% of these cases, including one CC. Among women identified with high-grade lesions, 37% (17/46) tested positive for tetravalent vaccine HR-types (HPV-16, 18), 65% (30/46) for nonavalent-vaccine HR-types (9v, HPV-16, 18, 31, 33, 45, 52, 58). Adding HPV35 to the nonavalent vaccine formulation potentially increases coverage to 80% (37/46) (100% considering only CC). Preliminary findings suggest high acceptability and good overall performance of the screening algorithm. However, several challenges emerged that may affect feasibility, including a proportion of invalid HPV test results or inconclusive outcomes in VIA assessment, and difficulties in ensuring referral compliance for women requiring further management.

CONCLUSION

This project provides fundamental evidence to enhance cervical cancer prevention efforts in Eswatini in two critical areas. The first is the support to the validity of the non-invasive urine-based screening methods. The second is the detection of a high prevalence of HPV 35 genotype and the consequent need to revisit formulation of available vaccines. Urine-based HR-HPV rapid testing proved feasible, acceptable and well-received. The study enabled the identification of critical underperforming steps and the development of corresponding solutions. A high frequency of invalid Xpert results was addressed by re-training laboratory personnel in the proper preparation of the sample. The failure of VIA to recognise presence of cervical lesions as compared with the effectiveness of the rapid molecular testing in detecting HR genotypes raises concerns about the future usefulness of VIA. The slow recruitment rate at the start could be addressed via engagement of community workers and leaders. Our findings also revealed that HPV35 is highly prevalent in high-grade lesions in Eswatini, accounting for 15% as the sole oncogenic genotype in 15% of these cases, including one CC. Current HPV vaccines do not include coverage of HPV35: such coverage could extend protection to a high proportion of AGW and further research is warranted to assess the type-specific CC burden in Sub-Saharan Africa.

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DOI: 10.54103/2282-0930/29181