NIRESHNI MITCHEV

PROJECT: Development of rapid point-of-care assays for the detection of curable sexually transmitted infections

Background and rationale:

Sexually transmitted infections (STIs) are a global public health concern as these infections negatively impact sexual and reproductive health (1). An estimated 1 million new STIs (chlamydia, gonorrhoea, trichomoniasis and syphilis) are acquired each day (2), with 376.4 million new cases of curable STIs occurring every year (1-3), and the majority of these are asymptomatic (1). World Health Organization Africa region prevalence statistics for women is; chlamydia 3.7%, gonorrhoea 1.7%, trichomoniasis 11.5% and syphilis 1.8%; (4). South African public health facilities treated 1.14 million new cases of symptomatic STIs in 2015-2016 (5).

The long term sequelae of STIs include; increasing the risk of HIV acquisition, cervical cancer deaths, pelvic inflammatory disease and infertility in women, mother-child transmission of STIs can result in stillbirth, low birth weight, prematurity, sepsis, pneumonia, neonatal conjunctivitis and congenital deformities (1). In the South African public health sector and other developing countries, STIs are treated using syndromic management (6). This non-laboratory approach utilises empiric treatment based on commonly known pathogens that cause clinical syndromes, without confirmation of the causative agent. The pathogen is therefore unknown and often there is no laboratory testing for cure determining whether treatment was successful until the patient returns with recurring symptoms and treatment failure. This also means that transmission of the infections continues. This is also an indication that the strains being transmitted are resistant to the current drug regimen. Syndromic management was implemented in the South African health system in 1995, and the prevalence of STI causing organisms and adverse events remains unchanged (7, 8).

Diagnostic surveillance is essential for STIs control, especially in high HIV incidence settings. Nucleic acid amplification tests (NAATs) technology is ideal for screening both symptomatic and asymptomatic patients. In our previous research, we have shown that there is an

opportunity for diagnosis-based treatment of STIs in low-middle-income-countries (9) and that point-of-care (POC) testing together with immediate treatment effectively reduced genital inflammation, potentially reducing the risk of HIV acquisition (10). We have also evaluated numerous commercially available molecular diagnostic assays which are accurate, sensitive, and specific (11, 12). These assays could fit well as near patient tests, however, most are not affordable for the large-scale public health sector.

Women's health must be a priority to reduce adverse events associated with STIs. We have developed an affordable, accurate, locally designed and manufactured STIs detection assay, which will be a step forward in STIs management and control. The test has the potential to optimize patient care and reduce the burden on the public health care system in the long-term. This will be a pilot study to evaluate the performance of the innovation to diagnose STIs in adolescent girls and young women in South Africa.

Study Design and scope:

This will be a prospective study of clinical specimens to detect STIs pathogens using real-time PCR. An ethics application will be submitted to the University of KwaZulu-Natal (UKZN) Biomedical Research Ethics Committee for approval. Vaginal swab specimens will be collected. Specimens will then be transported to the Medical Microbiology department at UKZN. *Neisseria gonorrhoea*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and Syphilis will be screened for, using the innovation prototype assay and validated against a commercially available diagnostic assay. SPSS statistical software will be used to determine tests performance characteristics. Dissemination of results by publication and conference.

Aim:

To evaluate the test performance characteristics and validate the prototype multiplex assay in a patient cohort, to detect STI-causing pathogens.

Primary Objective:

To determine the diagnostic sensitivity and specificity of the prototype multiplex assay for the in-vitro qualitative detection of *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and Syphilis in vaginal swab specimens from patients suspected of having STIs, in comparison with a commercially available assay.

References:

1. WHO. WHO factsheet 2021 [updated November 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis).
2. Rowley J, Vander Hoorn S, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bulletin of the World Health Organization. 2019;97(8):548.
3. Organization WH. Global health sector strategy on sexually transmitted infections, 2016–2021. Report Geneva. 2016.
4. Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, et al. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. PloS one. 2015;10(12):e0143304.
5. Council SANA. National Strategic Plan on HIV, STIs and TB (2017—2022). 2017.
6. STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINES LIST FOR SOUTH AFRICA.
7. White RG, Moodley P, McGrath N, Hosegood V, Zaba B, Herbst K, et al. Low effectiveness of syndromic treatment services for curable sexually transmitted infections in rural South Africa. Sexually transmitted infections. 2008;84(7):528-34.
8. Garrett NJ, McGrath N, Mindel A. Advancing STI care in low/middle-income countries: has STI syndromic management reached its use-by date? : BMJ Publishing Group Ltd; 2016.
9. Garrett NJ, Osman F, Maharaj B, Naicker N, Gibbs A, Norman E, et al. Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries. PLOS ONE. 2018;13(4):e0196209.
10. Garrett N, Mtshali A, Osman F, Masson L, McKinnon LR, Singh R, et al. Impact of point-of-care testing and treatment of sexually transmitted infections and bacterial vaginosis on genital tract inflammatory cytokines in a cohort of young South African women. Sexually Transmitted Infections. 2021.
11. Garrett N, Mitchev N, Osman F, Naidoo J, Dorward J, Singh R, et al. Diagnostic accuracy of the Xpert CT/NG and OSOM Trichomonas Rapid assays for point-of-care STI testing among young women in South Africa: a cross-sectional study. BMJ open. 2019;9(2):e026888.
12. Mitchev N, Singh R, Garrett N, Ramsuran V, Niehaus AJ, Mlisana KP. Performance of TaqMan probes for the detection of sexually transmitted infections in South African women. African Journal of Laboratory Medicine. 2021;10(1):4.