Innovating the fight against syphilis: SIM Project

Inovando a luta contra a sífilis: Projeto SIM

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ABSTRACT

Introduction: Syphilis is a major public health problem. Its incidence has increased in Brazil, particularly in the Southern Region. New tools are available, and immediate action is necessary. **Objective:** To describe the pilot study of an investigation aimed to assess the prevalence of syphilis, hepatitis B and C, and HIV and evaluate three strategies for adherence to syphilis treatment. **Methods:** A spontaneous sample of participants was evaluated with a structured questionnaire and underwent rapid tests for syphilis, HIV, and hepatitis B and C after signing an informed consent form (ICF). Rapid tests reagent for syphilis were confirmed by quantitative venereal disease research laboratory (VDRL) and *Treponema pallidum* hemagglutination assay (TPHA). Participants with confirmation of syphilis were randomized into three groups for follow-up: telephone calls, SIM app, and usual care at the health unit. **Results:** During a two-day pilot, 68 participants were included. Fourteen (20.6%) had tests reagent for syphilis, 1 (1.5%) for hepatitis B, 3 (4.4%) for hepatitis C, and 1 (1.5%) for HIV. Eight (57.1%) of the initial 14 individuals with rapid tests reagent for syphilis agreed to participate in the study. Out of the 8 rapid tests for syphilis, 2 (25%) were confirmed as active syphilis (>1/8). **Conclusion:** The prevalence of active syphilis estimated in this population was 3.5%. The demand for tests was high. The COVID-19 epidemic had a negative impact on the development of the study, which is ready for implementation. Discussions on the role of such a testing unit and the coverage of the research project in a context that requires increasing COVID-19-focused testing are fundamental for the future development of the project.

Keywords: syphilis; syphilis serodiagnosis; prevalence.

RESUMO

Introdução: A sífilis é um importante problema de saúde pública. A incidência tem aumentado no Brasil, principalmente na Região Sul. Novas ferramentas estão disponíveis e uma ação imediata é necessária. **Objetivo:** Descrever o estudo piloto de uma pesquisa que avalia a prevalência de sífilis, hepatites B e C e HIV e três estratégias de aderência ao seguimento do tratamento. **Métodos:** Uma amostra espontânea de participantes foi avaliada com um questionário estruturado e testes rápidos para sífilis, HIV e hepatites B e C foram realizados após assinatura do Termo de Consentimento Livre e Esclarecido (TCLE). Os testes rápidos reagentes para sífilis foram confirmados por VDRL (*venereal disease research laboratory*) quantitativo e hemaglutinação para sífilis (*Treponema pallidum hemagglutination assay* – TPHA). Os participantes com confirmação de sífilis foram randomizados em três grupos para acompanhamento: ligações telefônicas, aplicativo do SIM e cuidados habituais na unidade de saúde. **Resultados:** Durante um piloto de dois dias, 68 participantes foram incluídos. Quatorze (20,6%) tiveram testes reagentes para sífilis, 1 (1,5%) para hepatite B, 3 (4,4%) para hepatite C e 1 (1,5%) para HIV. Oito (57,1%) dos 14 casos iniciais com teste rápido reagente para sífilis aceitaram participar do estudo. Dos 8 testes rápidos para sífilis, 2 (25%) foram confirmados como sífilis ativa (>1/8). **Conclusão:** A prevalência de sífilis ativa estimada nesta população foi de 3,5%. A demanda por exames foi alta. A epidemia de COVID-19 impactou negativamente o desenvolvimento do estudo, que está pronto para implementação. A discussão sobre o papel desta espécie de unidade de teste e a abrangência do projeto de pesquisa em um contexto que pede a expansão de testes focados na COVID-19 são fundamentais para o desenvolvimento futuro do projeto.

Palavras-chave: sífilis; sorodiagnóstico da sífilis; prevalência.

INTRODUCTION

Syphilis infection has recently resurfaced as a significant public health problem[1]. The estimated global incidence of syphilis is 6.3 million (95% uncertainty interval – 95%UI: 5.5–7.1 million) cases every year[2]. Although preventable and treatable, this infection has persisted for centuries due to behavioral and structural factors. Besides persistent facilitating factors throughout the world, the present situation has had the contribution of a number of syphilis outbreaks in North America, Europe, and Australia, primarily within sexual networks of men who have sex with men (MSM), and often associated with HIV co-infection or co-transmission[3]. This scenario was connected to the introduction of combined antiretroviral therapy (cART), which progressively changed the understanding of HIV infection as a non-fatal condition, and, more recently, to the use of ART to prevent HIV infection (pre-exposure prophylaxis – PrEP)[4].

Syphilis is a major contributor to stillbirth and infant morbidity and mortality[5].

In 2007, the World Health Organization (WHO) established a global initiative to eliminate mother-to-child transmission of syphilis linked to the elimination of mother-to-child transmission of HIV[6].

Elimination of mother-to-child transmission of syphilis is also part of the WHO Global Health Sector Strategy on Sexually Transmitted Infections 2016–2021, aiming to eliminate syphilis as a public health problem by 2030[7].

Progress is being made. A recent publication identified that "congenital syphilis decreased worldwide between 2012 and 2016, although maternal prevalence was stable." The authors concluded that "the estimated decrease in CS [congenital syphilis] case rates between 2012 and 2016 reflected increased access to ANC [antenatal care] and to syphilis screening and treatment" and that "achieving

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global CS elimination, however, will require improving access to early syphilis screening and treatment in ANC, clinically monitoring all women diagnosed with syphilis and their infants, improving partner management, and reducing syphilis prevalence in the general population by expanding testing, treatment and partner referral beyond ANC"[8]. The last statement (our underlining) confirms the need to create new approaches to expand syphilis testing.

Brazil faces a progressive increase in both acquired and congenital syphilis. Compulsory reporting data indicate that acquired syphilis rates escalated from 2.0 cases/100,000 inhabitants in 2010 to 58.1 cases/100,000 inhabitants in 2017[9].

Congenital syphilis had 24,666 cases (incidence rate of 8.6/1,000 live births) and was responsible for 206 deaths (mortality rate of 7.2/100,000 live births), with 49,013 cases of syphilis reported in pregnant women[10].

Although this growth occurred in all Brazilian regions[11,12], it was higher in the detection rate of the Southern Region. Several causes could be associated with this increase, such as a high number of sexual partners, no condom use, and lack of effective sexually transmitted infection (STI) care (including misdiagnosis and delayed treatment), leading to a larger number of untreated transmitters in the population. Non-treatment of sexual partners, resulting in the recontamination of the index case and continuing the contamination of other sexual partners, could also be an important issue. As to congenital syphilis, inadequate antenatal care (ANC) is a major extra factor in its increasing rates.

Rapid tests (RTs) are now widely available, making syphilis screening more accessible and allowing an earlier treatment start for those with positive results[10].

Epidemic control depends on broad strategies, which should start by gathering epidemiological information, elaborating edu-communication strategies[13-15], and expanding the scope of prevention and control through the development of creative partnerships.

We propose to evaluate syphilis prevalence and the effectiveness of three different follow-up strategies.

OBJECTIVE

To describe the pilot study of an investigation aimed to assess the prevalence of syphilis, hepatitis B and C, and HIV and evaluate three strategies for adherence to syphilis treatment.

METHODS

A spontaneous sample of participants, recruited through a mobile unit (**Figure 1**), answered a questionnaire and underwent RTs after signing an informed consent form (ICF). The cases with reagent RT had their blood collected for confirmatory examination (venereal disease research laboratory – VDRL/*Treponema pallidum* hemagglutination assay – TPHA) at the time and started treatment with penicillin. Participants with confirmation of syphilis were randomized into three groups for follow-up: telephone calls, SIM app, and usual care at the health unit.

RESULTS

During a two-day pilot, interrupted by the preventive measures of the COVID-19 epidemic, 68 participants, 30 women and 38 men, with a mean age of 46.8 (19–78) years, were included. Among the tests performed, 14 (20.6%) were reagent for syphilis, 1 (1.5%) for hepatitis B, 3 (4.4%) for hepatitis C, and 1 (1.5%) for HIV. Eight (57.1%) of the initial 14 individuals with RTs reagent for syphilis agreed to

Figure 1 – The SIM bus parked at downtown Porto Alegre, Bra

participate in the study. Out of the 8 RTs for syphilis, 2 (25%) were confirmed as active syphilis (>1/8). All cases were reported to the health authorities.

DISCUSSION

The first three days of the study were reduced to two due to the establishment of social distancing related to COVID-19 prevention measures. Like in all other parts of the world, population circulation was restricted, and the commerce closed. Whether closing a mobile health unit providing syphilis, HIV, and hepatitis testing was reasonable remains an open question difficult to answer. The addition of COVID-19 antigen testing could have contributed not only to COVID-19 control but also to the perception that other health issues do not stop when a new one emerges. During these two days, the demand widely exceeded expectations. The mobile unit was parked in a busy pedestrian area close to the central market. Some adjustments were made regarding the position of the bus. Long lines were formed, with the participants showing no signs of hesitation to be seen waiting for STI testing. This could be a sign that expanding testing outside ANC, which is necessary to tackle acquired and congenital syphilis, will not increase social barriers. The ways the population presently deals with sexuality has evolved and become more open, contrary to past times when sex was associated with shame and hidden in conversations and practices. The average time per patient was 16 minutes, and the unit worked from 9 a.m. to 6 p.m. (9 hours/day).

Some participants left and did not return for the RT results, as observed in other sites providing STI care. Mechanisms to decrease these losses will be explored, including a better waiting area with entertainment activities, reinforced educational measures, and risk counseling.

The reagent test rates surpassed the expected prevalence, indicating that reaching the planned sample will be possible.

The syphilis test results evidence the need to have a confirmatory non-treponemal test after the initial treponemal test. Using just the RT would overestimate the prevalence and lead to overtreatment. Syphilis testing strategies have changed since the advent of RTs using treponema antigens. Highly sensitive and specific, they indicate whether the person has present, past, or treated syphilis. A negative treponemal test after having treated syphilis is unusual. Having a quantitative non-treponemal test to confirm the results is of utmost importance. The well-established methodology to estimate syphilis incidence and prevalence only considers studies in which the sample is larger than 100 individuals, with known testing strategies, using treponemal and non-treponemal tests[16-19]. Diagnosis of active syphilis needs titers equal to or higher than 1:8. This is the measure that must be used to estimate the prevalence of active syphilis. Accurate clinical and sexual history, clinical examination, risk assessment, and contact management must complement individual management.

The strengths of this study include innovation in syphilis follow-up methodologies; mobile unit capable of testing a high number of subjects in different geographical areas and in a short period; identification of syphilis, HIV, and hepatitis prevalence in the general population.

Among the limitations of this investigation, we underline the small sample due to its pilot phase; interruption caused by the COVID-19 control measures.

CONCLUSION

The prevalence of active syphilis estimated in this population was 3.5%. The demand for tests was high. The COVID-19 epidemic had a negative impact on the development of the study, which is ready for implementation. Discussions on the role of such a testing unit and the coverage of the research project in a context that requires increasing COVID-19-focused testing are fundamental for the future development of the project.

Participation of each author

Vanessa Martins de Oliveira: protocol development, project coordination, manuscript review. Antonio Gerbase: manuscript drafting, syphilis and public health advisor to the project. Suelen Porto Basgalupp: laboratory coordination, protocol development, manuscript review. Thayane Martins Dornelles: patient interview and care, protocol development, manuscript review. Emerson Silveira de Brito: patient interview and care, protocol development, manuscript review. Michele Paula Pretto: administrative coordination, protocol development, manuscript review. Luana Giongo Pedrotti: statistician, protocol development, manuscript review. Eliana Wendland: head of the project, protocol development, manuscript review.

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Conflict of interests

The authors declare no conflict of interests.

REFERENCES

1. Kitayama K, Segura ER, Lake JE, Perez-Brumer AG, Oldenburg CE, Myers BA, et al. Syphilis in the Americas: a protocol for a systematic review of syphilis prevalence and incidence in four high-risk groups, 1980–2016. Syst Rev. 2017;6:195. https://dx.doi.org/10.1186%2Fs13643-017-0595-3
2. Rowley J, Hoorn SV, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ. 2019;97(8):548-62. https://dx.doi.org/10.2471%2FBLT.18.228486
3. Australasian Sexual Health Alliance. Australian STI Guidelines for use in Primary health care [Internet]. Australasian Sexual Health Alliance; 2018 [accessed on Oct. 27, 2020]. Available at: http://www.sti.guidelines.org.au/sexually-transmissible-infections/syphilis
4. Cusini M, Ghislanzoni M, Bernardi C, Carminati G, Zerboni R, Alessi E, et al. Syphilis outbreak in Milan, Italy. Sex Transm Infect. 2004;80(2):154. https://dx.doi.org/10.1136%2Fsti.2003.007526
5. Canto SVE, Leite Araújo MA, Miranda AE, Cardoso ARP, Almeida RLF. Fetal and infant mortality of congenital syphilis reported to the Health Information System. 2019;14(3):e0213214. https://doi.org/10.1371/journal.pone.0209906
6. World Health Organization. Elimination of mother-to-child transmission (EMTCT) of HIV and syphilis. Global guidance on criteria and processes for validation. Geneva: World Health Organization; 2014.
7. World Health Organization. Global health sector strategy on sexually transmitted infections 2016–2021. Towards ending STIs. Report. Geneva: World Health Organization; 2016.

8. Korenromp EL, Rowley J, Alonso M, Mello MB, Wijesooriya NS, Mahiané SG, et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes—Estimates for 2016 and progress since 2012. 2019;14(7):e0211720. https://doi.org/10.1371/journal.pone.0211720
9. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das Doenças Sexualmente Transmissíveis, Aids e Hepatites, Virais. Manual Técnico para Diagnóstico da Sífilis [Internet]. Brasil: Ministério da Saúde; 2016 [accessed on Sept. 7, 2020]. 52 p. Available at: http://www.aids.gov.br/en/node/59218
10. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle. Boletim Epidemiológico de Sífilis. Brasil: Ministério da Saúde; 2017.
11. Silva PS, Vieira CSA, Gomes LMX, Barbosa TLA. Gestational and congenital syphilis in a municipality in Brazil between 2014 and 2018. DST - J Bras Doenças Sex Transm. 2019;31(4):112-7. https://doi.org/10.5327/DST-2177-8264-201931402
12. Farias RO, Lopes IMD, Santos LG, Dantas ASC. The reality of 13 years of prenatal care to pregnant women with syphilis in Sergipe state (2007-2019). DST - J Braz Doenças Sex Transm. 2019;31(4):123-30. https://doi.org/10.5327/DST-2177-8264-201931404
13. Huang D, Sangthong R, McNeil E, Chongsuvivatwong V, Zheng W, Yang Z. Effects of a phone call intervention to promote adherence to antiretroviral therapy and quality of life of HIV/AIDS patients in Baoshan, China: a randomized controlled trial. AIDS Res Treat. 2013;2013:580974. https://doi.org/10.1155/2013/580974
14. Sabin LL, DeSilva MB, Gill CJ, Zhong L, Vian T, Xie W, et al. Improving adherence to antiretroviral therapy with triggered real time text message reminders: the China through technology study (CATS). J Acquir Immune Defic Syndr. 2015;69(5):551-9. https://doi.org/10.1097/qai.0000000000000651
15. Swendeman D, Ramanathan N, Baetscher L, Medich M, Scheffler A, Comulada WS, et al. Smartphone self-monitoring to support self-management among people living with HIV: Perceived benefits and theory of change from a mixed-methods randomized pilot study. J Acquir Immune Defic Syndr. 2015;69(Suppl. 1):S80-91. https://doi.org/10.1097/qai.0000000000000570
16. Gerbase AC, Rowley JT, Heymann DH, Berkley SF, Piot P. Global prevalence and incidence estimates of selected curable STDs. Sex Transm Infect. 1998;74(Suppl. 1):S12-6.
17. World Health Organization. Report on global sexually transmitted infection surveillance. Geneva: WHO; 2018.
18. Newman L, Rowley J, Hoorn SV, 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. https://doi.org/10.1371/journal.pone.0143304
19. Ham DC, Lin C, Newman L, Wijesooriya NS, Kamb M. Improving global estimates of syphilis in pregnancy by diagnostic test type: a systematic review and meta-analysis. Int J Gynecol Obstet. 2015;130(Suppl. 1):S10-4. https://doi.org/10.1016/j.ijgo.2015.04.012

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