Population-based screening for acute SARS-CoV-2 infection using rapid antigen testing and the 5% pre-test probability. Is the specificity our problem?

Cribados en la infección por SARS-CoV-2 empleando pruebas rápidas de antígenos en poblaciones con baja prevalencia (<5%). ¿Es la especificidad nuestro problema?

WHO's overall objective against COVID-19 is to control the pandemic situation by reducing the spread and the mortality associated with it. In order to slow down the transmission is the key to actively search for infected patients and subsequently isolate them and track and place their contacts in quarantine.[1] The high percentage of asymptomatic patients together with the transmission before the onset of the symptoms make this search particularly complex. However, the screening strategy in the asymptomatic population is still controversial and its efficacy has not been well-established.

The following are the results of a population-based screening for asymptomatic SARS-CoV-2 infected patients in a high-transmission community (cumulative incidence 14 days 908.05) and a low-traceability (16.55%). Through local social media, all inhabitants (31,068) in the municipality tested (San Andrés del Rabanedo, León, Spain) who did not have any symptoms and had not experienced SARS-CoV-2 infection over the last 3 months were contacted and summoned in a sport center. Nasopharyngeal samples were taken with a swab and tested using the Panbio COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostic Jena GmbH) (sensitivity 93.3% and specificity 99.4% according to manufacturer specifications). When invalid results occurred, performing a new test was strongly recommended. All positive cases were invited to allow for a new nasopharyngeal sample on the same day to perform a confirmatory rRT-PCR test. RNA extraction was performed with the Applied Biosystems MagMAX Viral/Pathogen kit using an automated instrument (Thermo Scientific™ KingFisher™) and rRT-PCR was carried out on a QuantStudio 5 system (Applied Biosystems) using a commercial kit (TaqPath COVID-19 CE-IVD RT-PCR Kit, Applied Biosystems) targeting ORF1ab, N and S genes of SARS-CoV-2.

Rapid antigen testing (RAT) was carried out on 8187 people (Table 1). The result was invalid in six samples (none agreed to perform a second test), negative in 8127 and positive in 54 (apparent prevalence 0.66%). No significant differences were observed in the prevalence by sex or age. Of the 54 RAT positive participants, 51 were confirmed using rRT-PCR and three did not agree to have a new sample taken for confirmation. The positive predictive value of the RAT among those who agreed to a confirmatory test (51/51) was 100% as well as the specificity. In the worst scenario, if we assume that the three cases that did not access the rRT-PCR test were not confirmed, the specificity would have been 99.96% (95% CI 99.91–100%).

In spite of being an area with significant community transmission, the pre-test probability in the investigated area was very low and far below the 5% recommended by WHO to carry out screenings.[2] Nevertheless, a 100% specificity such as the one found in this screening program and also previously reported in a situation of low pre-test probability[3] or among asymptomatic close contacts[4] has resulted in a very acceptable performance as all cases detected were sources of SARS-CoV-2 infection.

The average number of threshold cycles (Ct) in the positive cases which underwent rRT-PCR confirmation (considering Cts for N gene) is also worth pointing out. It was 19.0 (SD 3.3) ranging from 13.7 to 29.6, even lower than that reported by other authors in symptomatic patients.[3] As previously proposed, samples containing small amounts of virus are most probably classified as negatives using RAT.[5] According to this, even in the case of low sensitivity, it could be assumed that false negatives in the RAT are cases with low viral loads and therefore with a limited relevance as sources of infection.[6,7]

To sum up, we report a high RAT specificity in a mass population screening in real life in a pre-test probability of less than 5%. Although the number of positive samples was limited, our results suggest a high yield of population screening strategies against COVID-19. Moreover, since the screening was organized by the Primary Care Services, all the isolating, care and tracing activities for cases and close contacts was interconnected.[8,9] Furthermore, as stated by Mina et al., it is not only the internal validity of a single diagnostic test which should be assessed[10]; the context of its use and the assessment within a *swiss cheese strategy* should also be taken into account when setting pre-test probabilities and rethinking the 5% as being a turning point to implement population screening strategies in asymptomatic people.

Table 1
Population distribution among surveyed, screened and rapid antigen test (RAT) positive individuals and SARS-CoV-2 infection prevalence detected by age and sex.

Variables	Surveyed		Screened		Apparent prevalence		
	No.	%	No.	%	Positives	%	95% CI
Age							
0–17	2412	7.76	555	23.1	1	0.18	0.05–1.00
18–64	19,080	61.41	5335	28.0	47	0.88	0.65–1.17
65–74	2794	8.99	872	31.2	2	0.23	0.03–0.82
≥75	2881	9.27	421	14.6	1	0.24	0.01–1.32
NR	3901	12.56	998	25.6	3	0.30	0.06–0.88
Sex							
Men	12,692	40.85	3062	24.1	26	0.85	0.56–1.24
Women	14,475	46.59	4121	28.5	25	0.61	0.39–0.89
NR	3901	12.56	998	25.6	3	0.30	0.06–0.88
Total							
	31,068	100	8187	26.35	54	0.66	0.5–0.86

NR, not registered.

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Bibliografía

1. World Health Organization. Covid-19 strategy update. https://www.who.int/docs/default-source/coronaviruse/covid-strategy-update-14april2020.pdf?sfvrsn=29da3ba0_19&download=true [updated 14.4.20, accessed 4.2.21].
2. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays. https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays [published 11.9.20, accessed 14.11.20].
3. Linares M, Pérez-Tanoira R, Carrero A, Romanyk J, Pérez-García F, Gómez-Herruz P, et al. Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms. J Clin Virol. 2020;133:104659, http://dx.doi.org/10.1016/j.jcv.2020.104659.
4. Torres I, Poujois S, Albert E, Colomina J, Navarro D. Evaluation of a rapid antigen test (Panbio™ COVID-19 Ag rapid test device) for SARS-CoV-2 detection in asymptomatic close contacts of COVID-19 patients. Clin Microbiol Infect. 2021;27:636.e1–4, http://dx.doi.org/10.1016/j.cmi.2020.12.022.
5. Yamayoshi S, Sakai-Tagawa Y, Koga M, Akasaka O, Nakachi I, Koh H, et al. Comparison of rapid antigen tests for COVID-10. Viruses. 2020;12:1420, http://dx.doi.org/10.3390/v12121420.
6. Tromberg BJ, Schwetz TA, Pérez-Stable EJ, Hodes RJ, Woychik RP, Bright RA, et al. Rapid scaling up of Covid-19 diagnostic testing in the United States—the NIH RADx initiative. N Engl J Med. 2020;383:1071–7, http://dx.doi.org/10.1056/NEJMsr2022263.
7. Pekosz A, Cooper C, Parvu V, Li M, Andrews JC, Manabe YC, et al. Antigen-based testing but not real-time PCR correlates with SARS-CoV-2 virus culture. Clin Infect Dis. 2021, http://dx.doi.org/10.1093/cid/ciaa1706ciaa1706.
8. Bellmunt JM, Caylà JA, Millet JP. Contact tracing in patients infected with SARS-CoV-2. The fundamental role of Primary Health Care and Public Health. Semergen. 2020;46 Suppl. 1:55–64, http://dx.doi.org/10.1016/j.semerg.2020.06.001.
9. Delgado-Rodríguez M, Martín-Sánchez V, Martínez-González MA. Cribados. In: Martínez-González MA, editor. Conceptos de salud pública y estrategias preventivas. 2da Edición Barcelona: Elsevier; 2018. p. 67–71.
10. Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 test sensitivity—a strategy for containment. N Engl J Med. 2020;383:e120, http://dx.doi.org/10.1056/NEJMp2025631.

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Infección de prótesis de rodilla por *Streptococcus gallolyticus* subsp. *gallolyticus*

Streptococcus gallolyticus *subsp.* gallolyticus *knee periprosthetic joint infection*

El complejo *Steptococcus bovis/equinus* (CSB), en especial *Streptococcus gallolyticus* subsp. gallolyticus, ha suscitado interés en los últimos años debido a la asociación encontrada entre las infecciones por este microorganismo y el cáncer colorrectal[1]. A continuación presentamos un caso infrecuente, una infección de prótesis de rodilla por *S. gallolyticus* subsp. *gallolyticus.*

Se trata de una paciente de 67 años con artroplastia total de rodilla izquierda implantada en 2016 por gonartrosis. En 2019 consultó por gonalgia progresiva de 12 meses de evolución sin antecedente traumático, llevaba 2 años sin dolor desde la intervención. En la exploración inicial se apreciaban signos flogóticos, con una PCR de 6,4 mg/dl. Ante la sospecha de infección protésica, se realizó artrocentesis diagnóstica, obteniéndose líquido de aspecto turbio, con una glucosa de 142 mg/dl y proteínas de 4,6 g/dl (no fue posible realizar recuento celular por líquido hemático y viscoso). A las 48 h se informó de crecimiento de *S. gallolyticus* subsp. *gallolyticus* (sensible a penicilina, cefotaxima y vancomicina; resistente a clindamicina y levofloxacino). Seis meses antes se le había realizado una colonoscopia con polipectomía de un adenoma tubulovelloso con displasia de bajo grado.

Se realizó cirugía en 2 tiempos. En el primer tiempo se realizó extracción de la prótesis con desbridamiento, lavado y colocación de un espaciador Biofix con antibiótico (vancomicina más gentamicina). Tras la obtención de muestras intraoperatorias se inició ceftriaxona 2 g/12 h. En estas se aisló *S. gallolyticus* subsp. *gallolyticus* con el mismo antibiograma que en el líquido sinovial. Presentó evolución favorable tras la intervención, completándose 14 días de tratamiento parenteral, y posteriormente amoxicilina 1 g/8 h oral, que realizó durante 8 semanas. Durante el ingreso se realizó un ecocardiograma transtorácico, sin obtenerse imágenes indicativas de endocarditis, con hemocultivos antes del inicio de antibioterapia negativos, y una ecografía abdominal que fue normal.

Transcurridos 6 meses, se realizó el segundo tiempo. Se implantó una artroplastia total de rodilla con profilaxis prequirúrgica con ceftriaxona más teicoplanina. Se mantuvo antibioterapia con ceftriaxona, que se suspendió tras una semana al ser negativos los cultivos de las muestras intraoperatorias. La paciente realiza seguimiento ambulatorio, sin incidencias.

El CSB está compuesto por 7 especies distinguidas por técnicas de biología molecular, con reciente cambio en su taxonomía: *S. equinus, S. alactolyticus, S. gallolyticus* subsp. *gallolyticus* (biotipo I), *S. gallolyticus* subsp. *macedonicus, S. gallolyticus* subsp. *pasteurianus* (biotipo II/2), *S. infantarius* subsp. *infantarius* (biotipo II/1) y *S. infantarius* subsp. *coli* (biotipo II/1)[2]. El interés de esta distinción está en que el biotipo que parece asociarse con una mayor frecuencia al cáncer de colon es el biotipo I (*S. gallolyticus* subsp. *gallolyticus*)[1].

Son cocos grampositivos, anaerobios facultativos, catalasa y oxidasa negativos, que expresan el antígeno D de Lancefield en su pared celular. Forman parte de la microbiota intestinal en un 5-16%