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.

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

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

The *Streptococcus bovis/Streptococcus equinus* complex (SBSEC), in particular *Streptococcus gallolyticus* subsp. *gallolyticus*, has generated interest in recent years in light of the link detected between infections with this micro-organism and colorectal cancer.[1] Below we report an uncommon case: a periprosthetic knee infection with *S. gallolyticus* subsp. *gallolyticus*.

A 67-year-old patient underwent a total left knee replacement in 2016 due to knee osteoarthritis. In 2019, she sought care for gradually worsening knee pain over the past 12 months with no history of trauma, after having been pain-free for two years following her operation. Initial examination revealed signs of inflammation, with a C-reactive protein (CRP) level of 6.4 mg/dl. Periprosthetic infection was suspected, and therefore diagnostic arthrocentesis was performed. This procedure yielded a cloudy fluid with glucose 142 mg/dl and protein 4.6 g/dl (the bloody and viscous nature of the fluid precluded a cell count). After 48 h, growth of *S. gallolyticus* subsp. *gallolyticus* (sensitive to penicillin, cefotaxime and vancomycin and resistant to clindamycin and levofloxacin) was reported. Six months earlier, the patient had undergone a colonoscopy involving polypectomy of a tubulovillous adenoma with low-grade dysplasia.

Surgery was performed in two stages. The first stage included prosthesis removal with debridement, lavage and placement of a BioFix spacer with antibiotics (vancomycin plus gentamicin). After intraoperative samples had been collected, ceftriaxone 2 g/12 h was started. *S. gallolyticus* subsp. *gallolyticus* was isolated in these samples and found to have the same antibiogram as in the synovial fluid. The patient followed a favourable course after the operation, completing 14 days of parenteral treatment, followed by oral amoxicillin 1 g/8 h for eight weeks. During admission, she underwent a transthoracic echocardiogram, which yielded no imaging indicative of endocarditis, as well as blood cultures before starting antibiotic therapy, which came back negative, and an abdominal ultrasound, which was normal.

The second stage of the surgery was performed six months later. The patient was given preoperative prophylaxis with ceftriaxone plus teicoplanin, and a total knee replacement was performed. Antibiotic therapy with ceftriaxone was maintained, then discontinued after one week in light of negative results for cultures of intraoperative samples. The patient was followed up on an outpatient basis without incident.

The SBSEC comprises seven species distinguished using molecular biology techniques, with a recent change in taxonomy: *S. equinus, S. alactolyticus, S. gallolyticus* subsp. *gallolyticus* (biotype I), *S. gallolyticus* subsp. *macedonicus, S. gallolyticus* subsp. *pasteurianus* (biotype II/2), *S. infantarius* subsp. *infantarius* (biotype II/1) and *S. infantarius* subsp. *coli* (biotype II/1).[2] The usefulness of this distinction lies in the fact that the biotype apparently associated with colon cancer at a higher rate is biotype I (*S. gallolyticus* subsp. *gallolyticus*).[1]

These catalase- and oxidase-negative micro-organisms are Gram-positive cocci and facultative anaerobes that express Lancefield antigen group D in their cell wall. They form part of the intestinal microbiota in 5%–16% of healthy adults. These micro-organisms have been linked to infections in animals and humans. They are causal agents of bacteraemia and endocarditis, as well as meningitis and urinary tract infections, biliary tract infections and osteoarticular infections. Arthritis is less common than spondylodiscitis.[3]

Periprosthetic knee infection is a serious complication with an incidence of 0.4%–3.9%.[4] Risk factors include immunosuppression, diabetes mellitus and malnutrition. The most commonly isolated

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