



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Carta al Editor

Comentarios al documento *Recomendaciones de cribado GEPI-SEIMC para pacientes con sospecha de estrongiloidosis*



Comments to the document *GEPI-SEIMC screening recommendations for patients with suspected strongyloidosis*

Sr. Editor:

Recientemente el Grupo de Estudio de Patología Importada (GEPI) de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) ha publicado en su página web un documento titulado *Recomendaciones de cribado GEPI-SEIMC para pacientes con sospecha de estrongiloidosis*¹. Aplaudimos la realización de este documento, extremadamente necesario para concienciar sobre la necesidad de cribar estrongiloidiasis en personas inmunodeprimidas o en riesgo de inmunosupresión, incluidas personas con infección por SARS CoV-2 que van a recibir tratamiento con corticoides y/u otros fármacos inmunosupresores^{2,3}, y para aportar recomendaciones sobre cómo realizar dicho cribado basadas en la evidencia científica actual. Sin embargo, hay varias apreciaciones que consideramos precisan puntualizarse.

En primer lugar, si bien coincidimos en que la técnica de elección para el cribado de la estrongiloidiasis es la serología, existen estudios que muestran una sensibilidad insuficiente de la misma en pacientes inmunodeprimidos⁴, por lo que se necesita más evidencia para poder recomendar la serología como única técnica de cribado en población inmunosuprimida. De hecho, las recomendaciones de las últimas guías basadas en la evidencia son combinar la serología con métodos parasitológicos en pacientes ya inmunodeprimidos⁵.

En segundo lugar y respecto a evitar el tratamiento empírico sistemático, existen evidencias científicas sólidas de que el tratamiento empírico presuntivo es una práctica coste-efectiva^{6,7}, e incluso ahorradora de costes, especialmente en pacientes inmunodeprimidos o en riesgo de inmunosupresión sin menoscabar los resultados en salud para los pacientes^{7,8}. Consideramos que dicha evidencia debe ser tomada en cuenta a la hora de establecer recomendaciones. Además, en muchos centros españoles, incluidos algunos de los situados en zonas endémicas de estrongiloidiasis en España⁹, no se dispone de dicha serología en el laboratorio local y los resultados tardan un tiempo inaceptablemente largo para retrasar el tratamiento de un paciente que se va a inmunosuprimir. Las recomendaciones actuales, realizadas previamente a la publicación de los estudios de coste-efectividad, son las de administrar un tratamiento empírico en pacientes inmunosuprimidos o candidatos a inmunosupresión si no se va a poder descartar la infección en un tiempo adecuado⁵. Consecuentemente, consideramos que esperar a que el paciente desarrolle manifestaciones de hiperinfestación o estrongiloidiasis diseminada para iniciar un tratamiento empírico es exponer al paciente a un riesgo innecesario. El tratamiento

empírico debe ir destinado, precisamente, a evitar el desarrollo del síndrome de hiperinfestación o infección diseminada. Además, una vez se ha producido este y el paciente tiene síntomas compatibles con hiperinfestación o con infección diseminada, la recomendación no debería ser el uso de ivermectina 200 mcg/kg en dosis única, pues esta es una pauta estudiada únicamente en personas inmunocompetentes sin enfermedad diseminada¹⁰.

Por todo lo anteriormente expuesto, agradecemos a GEPI-SEIMC la publicación de estas necesarias recomendaciones y esperamos que estas puntualizaciones sean tenidas en cuenta en las próximas versiones del documento.

Bibliografía

1. Recomendaciones de cribado GEPI-SEIMC para pacientes con sospecha de estrongiloidosis [Internet]. 2021 [consultado 27 Mar 2022]. Disponible en: https://www.seimc.org/ficheros/gruposdeestudio/gepi/Dcientificos/documentos/gepi-dc-2021-Recomendaciones.Cribado_Estrongiloidosis.pdf/5467-3568
2. Stauffer W, Alpern J, Walker P. COVID-19 and dexamethasone: A potential strategy to avoid steroid-related strongyloides hyperinfection. *JAMA* [Internet]. 2020;324:623–4 [consultado 27 Mar 2022]. Disponible en: <https://jamanetwork.com/journals/jama/fullarticle/2769100>.
3. De Wilton A, Nabarro LE, Godbole GS, Chiodini PL, Boyd A, Woods K. Risk of strongyloides hyperinfection syndrome when prescribing dexamethasone in severe COVID-19. *Travel Med Infect Dis*. 2021;40:101981.
4. Luvira V, Trakulhun K, Mungthin M, Naaglor T, Chantawat N, Pakdee W, et al. Comparative diagnosis of strongyloidiiasis in immunocompromised patients. *Am J Trop Med Hyg*. 2016;95:401–4.
5. Requena-Méndez A, Buonfrate D, Gomez-Junyent J, Zammarchi L, Bisoffi Z, Muñoz J. Evidence-based guidelines for screening and management of strongyloidiiasis in non-endemic countries. *Am J Trop Med Hyg*. 2017;97:645–52.
6. Muennig P, Pallin D, Randall S, Man-Suen C. Cost effectiveness of strategies for the treatment of intestinal parasites in immigrants. *N Engl J Med* [Internet]. 1999;340:773–9. <http://dx.doi.org/10.1056/NEJM199903113401006>.
7. Maskery B, Coleman MS, Weinberg M, Zhou W, Rotz L, Klosovsky A, et al. Economic analysis of the impact of overseas and domestic treatment and screening options for intestinal helminth infection among US-Bound refugees from Asia. *PLoS Negl Trop Dis* [Internet]. 2016;10:1–14. <http://dx.doi.org/10.1371/journal.pntd.0004910>.
8. Wikman-Jorgensen PE, Llenas-García J, Shedrawy J, Gascon J, Muñoz J, Bisoffi Z, et al. Cost-effectiveness of different strategies for screening and treatment of *Strongyloides stercoralis* in migrants from endemic countries to the European Union. *BMJ Glob Heal*. 2020;5:1–10.
9. Dato AL, Pacheco-Tenza MI, Brunete EB, López BM, López MG, Cuello IG, et al. Strongyloidiiasis in southern alicante (Spain): Comparative retrospective study of autochthonous and imported cases. *Pathogens*. 2020;9:1–11.
10. Buonfrate D, Salas-Coronas J, Muñoz J, Maruri BT, Rodari P, Castelli F, et al. Multiple-dose versus single-dose ivermectin for *Strongyloides stercoralis* infection (Strong Treat 1 to 4): a multicentre, open-label, phase 3, randomised controlled superiority trial. *Lancet Infect Dis* [Internet]. 2019;23 [consultado 27 Mar 2022]. Disponible en: <https://linkinghub.elsevier.com/retrieve/pii/S1473309919302890>.

Philip Wikman-Jorgensen^{a,*}, Ana Requena-Méndez^{b,c},
Miriam Navarro^{d,e} y Jara Llenas-García^{f,g}

^a Servicio de Medicina Interna, Hospital Universitario San Juan de Alicante-FISABIO, San Juan de Alicante, España

^b Instituto de Salud Global de Barcelona (ISGlobal, Hospital Clinic-University of Barcelona), Barcelona, España

^c Department of Medicine Solna, Karolinska Institutet, Solna, Suecia

^d Unidad de Epidemiología, Centro de Salud Pública de Elche, Alicante, España

^e Departamento de Salud Pública, Historia de la Ciencia y Ginecología; Universidad Miguel Hernández de Elche, Alicante, España

^f Servicio de Medicina Interna/infecciosas, Hospital Vega Baja-FISABIO, Alicante, España

^g Departamento de Medicina Clínica, Universidad Miguel Hernández de Elche, San Juan de Alicante, España

* Autor para correspondencia.

Correo electrónico: wikman_phi@gva.es (P. Wikman-Jorgensen).

<https://doi.org/10.1016/j.eimc.2022.02.011>

0213-005X/ © 2022 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

A systematic review on rapid antigen test devices for SARS-CoV-2 in nursing homes: Useful, but handle with care



Una revisión sistemática sobre los test rápidos de antígenos para la detección del SARS-CoV-2 en centros residenciales: útiles, pero deben manejarse con cuidado

Dear Editor,

The COVID-19 pandemic has disproportionately affected Nursing homes (NHs), with mortality rates largely exceeding those of the general population, particularly during the first wave.^{1,2} A recent study from England and Wales has estimated an 18-fold difference in mortality rates when figures were compared to the pre-pandemic time period, but this is a likely an underestimate given the low levels of testing in NHs, particularly when nasal swabs with subsequent Real-Time quantitative polymerase chain reaction (RT-qPCR) represented the only validated diagnostic items.²

As recently pointed out by Domínguez Fernandez et al.,³ rapid antigen tests (RAT), with their reduced costs and turnaround times,⁴ could significantly speed and scale up diagnoses, benefiting residents' and workers' safety. However, available evidence appears far more controversial. We specifically performed a systematic review and meta-analysis on RAT in NHs according to PRISMA guidelines (see [Annex 1A](#) for the detailed search strategy),⁵ being able to retrieve 5 studies ([Table 1](#)), for a total of 1327 paired samples RAT vs. RT-qPCR from residents of NHs, three of them from Spain.^{3,6–9}

Overall, RT-qPCR detected 337 SARS-CoV-2 positive cases (25.4%), with a pooled sensitivity of 75.8% (95% Confidence Interval [95%CI] 61.0–86.2) that was affected by substantial heterogeneity ($I^2 = 82%$, $p < 0.01$), and a pooled specificity of 99.0% (95%CI 89.3–99.9) (see [Annex 1B](#) for details). Two studies included estimates of viral replication,^{6,8} while other two studies reported RAT performances by symptom status.^{8,9} Even though Escrivá et al.⁷ included both symptom and viral activity statuses, reporting strategy impaired their inclusion in subgroup estimates. When sensitivity was calculated for samples characterized by cycle threshold values ≥ 25 , an overall estimate of 25.8% was calculated, that increased to 67.3% in asymptomatic individuals irrespective of their viral replication status.

Diagnostic agreement, reported by means of Cohen's Kappa, ranged between 0.377 (95%CI 0.352–0.401)⁸ and 0.927 (95%CI 0.909–0.944),³ with a pooled estimate of 0.670 (95%CI 0.452–0.889), suggesting a moderate agreement despite the substantial heterogeneity ($I^2 = 100%$, $p < 0.01$). Diagnostic Odds Ratio (DOR) was estimated in 95.552 (95%CI 16.125–565.859), i.e. the OR for the positive result among residents with SARS-CoV-2 was approximately 96 times higher than the OR for positive results among persons without SARS-CoV-2. Summary Receiver Operating Characteristic (SROC) Curve ([Annex 1C](#)) was estimated through a maximum likelihood estimation model (REML), and a fixed model. Not only both curves were quite asymmetrical, suggesting a substantial heterogeneity among retrieved studies, but the substantial difference between the curves suggested that a substantial threshold effect may present, i.e. higher content of viral antigen may lead to increased identification of positive cases by RAT.

In other words, real-world estimates suggest that actual reliability of RAT may be quite far from optimal, particularly for non-seriated testing strategy. As acknowledged by Domínguez-Fernández et al.,³ in cases characterized by high viral load, RAT may be quite reliable,^{6,8} but they exhibited substantial lack of sensitivity when employed in individuals that exhibit low viral replication. Indeed, RAT may be quite unreliable when employed to screen earlier stages of SARS-CoV-2 infections, or in individuals who, because of their even transitory lack of symptoms, may actively spread the infection not only among other residents, but also in NH workers failing to cope with appropriate preventive measures.^{1,2} As a consequence, as suggested by McKay et al.,⁹ early and frequent referral to RAT rather than a single and synchronous sampling campaign may be quite effective in identifying individuals with the greatest potential to transmit the virus.

In summary, as RAT are relatively easy to use, produce results in minutes, and do not require expensive laboratory instruments, they can provide actionable results, particularly during outbreaks, but require a rational and specifically tailored use. On the contrary, as previously stressed by Escrivá et al.,⁷ the improper referral to instruments that can be affected by substantial lack of sensitivity may lead to potentially dismal consequences.