Enfermedades Infecciosas y Microbiología Clínica 40 (2022) 411–414

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Letters to the Editor

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

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

Dear Editor:

Recently, the Grupo de Estudio de Patología Importada (GEPI) [Imported Pathology Study Group] of the Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC) [Spanish Society of Infectious Diseases and Clinical Microbiology] published a document on its website entitled GEPI-SEIMC screening recommendations for patients with suspected strongyloidosis.[1] We applaud the publication of this document, as it is vitally necessary to raise awareness of the need to screen for strongyloidiasis in the immunosuppressed or those at risk of immunosuppression, including people with SARS CoV-2 infection due to receive treatment with corticosteroids and/or other immunosuppressive drugs,[2,3] and to provide recommendations on how to perform such screening based on current scientific evidence. However, we believe a number of points need to be made.

First of all, while we agree that the technique of choice for screening strongyloidiasis is serology, there are studies that show that it presents insufficient sensitivity in immunosuppressed patients,[4] whereby more evidence is needed to recommend serology as the only screening technique in the immunosuppressed population. In fact, the recommendations of the latest evidence-based guidelines are to combine serology with parasitology methods in patients already immunosuppressed.[5]

Secondly, and with regard to avoiding systematic empirical treatment, there is solid scientific evidence that presumptive empirical treatment is a cost-effective,[6,7] and even cost-saving, practice, particularly in patients who are immunosuppressed or are at risk of immunosuppression, without undermining the health outcomes for the patients.[7,8] We believe that this evidence should be taken into account when establishing recommendations. In addition, in many Spanish centres, including some of those in areas of Spain where strongyloidiasis is endemic,[9] this serology is not available at the local laboratory and results take an unacceptably long time, considering the ensuing delay in initiating treatment in patients who are to be immunosuppressed. The current recommendations, issued prior to the publication of the cost-effectiveness studies, are to administer empirical treatment in immunosuppressed patients or candidates for immunosuppression if infection cannot be ruled out within an appropriate time.[5] We therefore believe that waiting for the patient to develop signs and symptoms of hyperinfestation or disseminated strongyloidiasis before starting empirical treatment exposes them to an unnecessary risk. Empirical treatment should be aimed precisely at preventing the development of hyperinfestation syndrome or disseminated infection. Moreover, once the patient presents symptoms consistent with hyperinfection or disseminated infection, the recommendation should not be the use of single-dose ivermectin 200 mcg/kg, as that regimen has only been studied in immunocompetent people without disseminated disease.[10]

In view of all the above, we thank the GEPI-SEIMC for publishing these necessary recommendations, and we hope that these points will be taken into account in future versions of the document.

References

1. Recomendaciones de cribado GEPI-SEIMC. para pacientes con sospecha de Estrongiloidosis [Internet]. 2021. 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. 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 strongyloidiasis 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 strongyloidiasis in non-endemic countries. Am J Trop Med Hyg. 2017;97(3):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. Disponible en: http://www.nejm.org/doi/abs/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. Disponible en: https://doi.org/10.1371/journal.pntd.0004910
8. Wikman-Jorgensen PE, Llenas-Garcia 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. Strongyloidiasis 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. Disponible en: https://linkinghub.elsevier.com/retrieve/pii/S1473309919302890

DOI of original article: https://doi.org/10.1016/j.eimc.2022.02.011

☆ Please cite this article as: Wikman-Jorgensen P, Requena-Méndez A, Navarro M, Llenas-García J, Comentarios al documento *Recomendaciones de cribado GEPI-SEIMC para pacientes con sospecha de estrongiloidosis*, Enferm Infecc Microbiol Clin. 2022;40:411–412.

Philip Wikman-Jorgensen [a,*], Ana Requena-Méndez [b,c], Miriam Navarro [d,e], Jara Llenas-García [f,g]

[a] *Servicio de Medicina Interna, Hospital Universitario San Juan de Alicante-FISABIO, San Juan de Alicante, Spain*
[b] *Barcelona Institute for Global Health (ISGlobal, Hospital Clinic-University of Barcelona), Barcelona, Spain*
[c] *Department of Medicine Solna, Karolinska Institutet, Solna, Sweden*
[d] *Unidad de Epidemiología, Centro de Salud Pública de Elche, Alicante, Spain*
[e] *Departamento de Salud Pública, Historia de la Ciencia y Ginecología, Universidad Miguel Hernández de Elche, Alicante, Spain*
[f] *Servicio de Medicina Interna/infecciosas, Hospital Vega Baja-FISABIO, Alicante, Spain*
[g] *Departamento de Medicina Clínica, Universidad Miguel Hernández de Elche, San Juan de Alicante, Spain*

* Corresponding author.
E-mail address: wikman_phi@gva.es (P. Wikman-Jorgensen).

https://doi.org/10.1016/j.eimce.2022.05.004

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 Dominguez-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.