

LETTERS TO EDITOR

## **COVID-19: The African enigma** COVID-19: El enigma de Africa

Robert Colebunders<sup>1</sup> robert.colebunders@uantwerpen.be

1 University of Antwerp, Global Health Institute, Antwerp, Belgium

Article: https://colombiamedica.univalle.edu.co/index.php/comedica/article/view/4613

We read with interest the paper by Guerrero *et al* "COVID-19: The Ivermectin African Enigma" <sup>1</sup>. In an ecological study they compared COVID-19 related mortality and infection rates between APOC (African Programme for Onchocerciasis Control) and non-APOC countries. After adjusting for Human Development Index (HDI) and number of performed test, COVID-19 mortality and infection rate were respectively 28% and 8% lower in non-APOC countries compared to APOC countries <sup>1</sup>. The authors suggested that this difference may be related to the community directed treatment with ivermectin (CDTI) programs established in APOC countries.

We agree that it remains to be explained why a lower COVID-19 mortality is observed in many APOC countries compared to other parts of the world. However, we do not believe that this is related to CDTI programs. Indeed, in APOC countries ivermectin is distributed only once (most countries) or twice a year <sup>2</sup>. Moreover, April 1<sup>st</sup> 2020, because of the COVID-19 pandemic, CDTI programs were interrupted and were only recently restarted <sup>2</sup>.

Ivermectin has an *in vitro* anti-COVID-19 effect <sup>3</sup> and also certain clinical trials suggested a beneficial effect of ivermectin on COVID-19 disease outcome <sup>4</sup>. However, in a recent small double blind, randomized control trial in Colombia, five days of ivermectin, at a 10 times the recommended dose, did not reduce the duration of symptoms of mild COVID-19 disease compared to placebo<sup>5</sup>. Given the half-life of ivermectin, approximately 18h<sup>6</sup>, it is unlikely that CDTI, only one dose of ivermectin once or twice a year, may be able to reduce COVID-19 related mortality.

Many factors could explain the lower COVID-19 mortality in APOC countries <sup>7</sup>. One of them could be exposure to parasitic infections and the immune response induced by these infections. For example, for *P. falciparum*, a parasitic infection highly prevalent in APOC countries, it has been hypothesised that the immunological memory against *P. falciparum* merozoites primes SARS-CoV-2 infected cells for early phagocytosis and therefore may protect persons with a recent *P. falciparum* infection against severe COVID-19 disease <sup>8</sup>. Helminth infections, such as onchocerciasis, may down regulate immune responses <sup>9</sup> and potentially inactivate the inflammatory signalling pathways that may induce acute respiratory distress syndrome (ARDS), one of the causes of death in COVID-19 infected persons <sup>10</sup>.



**Citation:** Colebunders R. **COVID-19: The African enigma.** Colomb Méd (Cali), 2021;

52(2):e7014816 <u>http://doi.</u> org/10.25100/cm.v52i2.4816

Copyright: © 2021 Universidad del Valle



Corresponding author:

**Robert Colebunders.** University of Antwerp, Global Health Institute, Antwerp, Belgium

e-mail: robert.colebunders@ uantwerpen.be



#### References

1. Guerrero R, Bravo LE, Muñoz E, Grillo AEK, Guerrero E. COVID-19: The Ivermectin African Enigma. Colomb Med (Cali). 2020; 51(4):e2014613. Doi: 10.25100/cm.v51i4.4613.

2. Hamley JID, Blok DJ, Walker M, Milton P, Hopkins AD, Hamill LC, et al. What does the COVID-19 pandemic mean for the next decade of onchocerciasis control and elimination? Trans R Soc Trop Med Hyg. 2021; 115(3): 269-80. doi: 10.1093/trstmh/traa193.

3. Rizzo E. Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. Naunyn Schmiedebergs Arch Pharmacol. 2020; 393(7): 1153-6. doi: 10.1007/s00210-020-01902-5.

4. Kow CS, Merchant HA, Mustafa ZU, Hasan SS. The association between the use of ivermectin and mortality in patients with COVID-19: a meta-analysis. Pharmacol Rep. 2021. doi: 10.1007/s43440-021-00245-z.

5. Lopez-Medina E, Lopez P, Hurtado IC, Dávalos DM, Ramirez O, Martínez E, et al. Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial. JAMA. 2021; e213071. doi: 10.1001/jama.2021.3071.

6. Gonzalez CA, Sahagun PAM, Diez LMJ, Fernandez MN, Sierra VM, Garcia VJJ. The pharmacokinetics and interactions of ivermectin in humans--a mini-review. AAPS J 2008; 10(1):42-6. doi: 10.1208/s12248-007-9000-9.

7. Njenga MK, Dawa J, Nanyingi M, Gachohi J, Ngere I, Letko M, et al. Why is There Low Morbidity and Mortality of COVID-19 in Africa? Am J Trop Med Hyg. 2020; 103(2): 564-9. doi: 10.4269/ajtmh.20-0474.

 Kalungi A, Kinyanda E, Akena DH, Kaleebu P, Bisangwa IM. Less Severe Cases of COVID-19 in Sub-Saharan Africa: Could Co-infection or a Recent History of Plasmodium falciparum Infection Be Protective? Front Immunol. 2021; 12: 565625. doi: 10.3389/fimmu.2021.565625.

9. McSorley HJ, Hewitson JP, Maizels RM. Immunomodulation by helminth parasites: defining mechanisms and mediators. Int J Parasitol. 2013; 43(3-4): 301-10. doi: 10.1016/j.ijpara.2012.11.011.

10. Choudhary S, Sharma K, Silakari O. The interplay between inflammatory pathways and COVID-19: A critical review on pathogenesis and therapeutic options. Microb Pathog. 2021; 150: 104673. doi: 10.1016/j. micpath.2020.104673.



LETTERS TO EDITOR

# Reply to a letter by Robert from Colebunders entitled COVID-19: The African Enigma

# Respuesta a una carta de Robert de Colebunders titulada COVID-19: The African Enigma

Rodrigo Guerrero<sup>1</sup>, Luis Eduardo Bravo<sup>2,3</sup>, Edgar Muñoz<sup>4</sup>, Elvia Karina Grillo Ardila<sup>5</sup>, Esteban Guerrero<sup>6</sup> luis.bravo@correounivalle.com

1 Universidad del Valle, Instituto de Investigación y Desarrollo en Prevención de la Violencia y Promoción de la Convivencia Social, CISALVA, Cali, Colombia., 2 Universidad del Valle, Facultad de Salud, Escuela de Medicina, Departamento de Patología, Cali, Colombia, 3 Registro Poblacional de Cáncer, Cali, Colombia. 4 University of Texas, Health Science Center San Antonio, Texas, USA.5 Universidad del Valle, Facultad de Salud, Doctorado en Salud, Cali, Colombia. 6 Barbara&Frick. Bogotá. Colombia.

Article: https://colombiamedica.univalle.edu.co/index.php/comedica/article/view/4613

We read with interest the paper by Guerrero et al "COVID-19: The Ivermectin African Enigma" <sup>1</sup>. In an ecological study they compared COVID-19 related mortality and infection rates between APOC (African Programme for Onchocerciasis Control) and non-APOC countries. After adjusting for Human Development Index (HDI) and number of performed test, COVID-19 mortality and infection rate were respectively 28% and 8% lower in non-APOC countries compared to APOC countries <sup>1</sup>. The authors suggested that this difference may be related to the community directed treatment with ivermectin (CDTI) programs established in APOC countries.

We agree that it remains to be explained why a lower COVID-19 mortality is observed in many APOC countries compared to other parts of the world. However, we do not believe that this is related to CDTI programs. Indeed, in APOC countries ivermectin is distributed only once (most countries) or twice a year <sup>2</sup>. Moreover, April 1<sup>st</sup> 2020, because of the COVID-19 pandemic, CDTI programs were interrupted and were only recently restarted <sup>2</sup>.

Ivermectin has an *in vitro* anti-COVID-19 effect<sup>3</sup> and also certain clinical trials suggested a beneficial effect of ivermectin on COVID-19 disease outcome <sup>4</sup>. However, in a recent small double blind, randomized control trial in Colombia, five days of ivermectin, at a 10 times the recommended dose, did not reduce the duration of symptoms of mild COVID-19 disease compared to placebo<sup>5</sup>. Given the half-life of ivermectin, approximately 18h<sup>6</sup>, it is unlikely that CDTI, only one dose of ivermectin once or twice a year, may be able to reduce COVID-19 related mortality.

Many factors could explain the lower COVID-19 mortality in APOC countries <sup>7</sup>. One of them could be exposure to parasitic infections and the immune response induced by these infections. For example, for *P. falciparum*, a parasitic infection highly prevalent in APOC countries, it has been hypothesised that the immunological memory against *P. falciparum* merozoites primes SARS-CoV-2 infected cells for early phagocytosis and therefore may protect persons with a recent *P. falciparum* infection against severe COVID-19 disease <sup>8</sup>. Helminth infections, such as onchocerciasis, may down regulate immune responses <sup>9</sup> and potentially inactivate the inflammatory signalling pathways that may induce acute respiratory distress syndrome (ARDS), one of the causes of death in COVID-19 infected persons <sup>10</sup>.



**Citation:** Guerrero R, Bravo LE, Muñoz Edgar, Grillo AEK, Guerrero E. **Reply to a letter by Robert from Colebunders entitled COVID-19: The African Enigma.** Colomb Méd (Cali),

2021; 52(2):e7024833 <u>http://doi.</u> org/10.25100/cm.v52i2.4833

Copyright: © 2021 Universidad del



**Conflicts of interest:** All authors contributed equally

#### Corresponding author:

Luis Eduardo Bravo. Universidad del Valle, Facultad de Salud, Escuela de Medicina, Departamento de Patología, Cali, Colombia. e-mail: luis.bravo@ correounivalle.com



Notes: 1. Torres Miyerlandi; Secretary of Health (Cali, Colombia). Official Communication.

### References

1. Guerrero R, Bravo L, Muñoz E, Grillo AE, Guerrero E. COVID-19: The Ivermectin African Enigma. Colomb Med (Cali). 2020; 51(4) : e2014613 DOI: 10.25100/cm.v51i4.4613.

2. Hellwig DM, Maia A. A COVID-19 prophylaxis? Lower incidence associated with prophylactic administration of ivermectin. Int J Antimicrob Agents. 2021;57(1): 106248. Doi: 10.1016/j.ijantimicag.2020.

3. Mbow M, Lell B, Jochems SP, Cisse B, Mboup S, Dewals BG, et al. COVID-19 in Africa: Dampening the storm? Science. 2020 ; 369(6504):624-626. doi: 10.1126/science.

4. López-Medina E, López P, Hurtado IC, Dávalos DM, Ramirez O, Martínez E, et al. Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial. JAMA. 2021; 325(14):1426-1435. doi: 10.1001/jama.2021.3071.