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Review article

The use of Ivermectin for the treatment of COVID-19: Panacea or enigma?

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ABSTRACT

The outbreak of SARS-CoV-2 pandemic has triggered unprecedented social, economic and health challenges. To control and reduce the infection rate, countries employed non-pharmaceutical measures such as social distancing, isolation, quarantine, and the use of masks, hand and surface sanitisation. Since 2021 a global race for COVID-19 vaccination ensued, mainly due to a lack of equitable vaccine production and distribution. To date, no treatments have been demonstrated to cure COVID-19. The scientific World is now considering the potential use of Ivermectin as a prophylactic and treatment for COVID-19. Against this background, the objective of this study is to review the literature to demystify the enigma or panacea in the use of Ivermectin. This paper intends to investigate literature which supports the existence or shows the nonexistence of a causal link between Ivermectin, COVID-19 mortality and recovery. There are inconsistent results on the effectiveness of Ivermectin in the treatment of COVID-19 patients. Some studies have asserted that in a bid to slow down the transmission of COVID-19, ivermectin can be used to inhibit the in vitro replication of SARS-CoV-2. The pre-existing health system burdens can be alleviated as patients treated prophylactically would reduce hospital admissions and stem the spread of COVID-19. On a global scale, Ivermectin is currently used by about 28% of the world's population, and its adoption is presently about 44% of countries. However, the full administration of this drug would require further tests to establish its clinical effectiveness and efficacy.

1. Introduction

Ivermectin is a macrocyclic lactone 22,23-dihydroavermectin B obtained from a gram-positive bacterium named *Streptomyces avermitilis* belonging to the genus Streptomyces.[1,2] Ivermectin is regarded as a miracle therapeutic drug in medicine because of its wider antiparasitic efficacy against ectoparasites and endoparasites.[3] Ivermectin's active spectrum is growing yearly, labelling it as one the most effective pharmaceuticals ever developed.[3] Also, Ivermectin has recently been used to reduce insect-borne diseases, including malaria.[1,3,4] The World Health Organization's Standard catalogue of valuable drugs includes Ivermectin4. Ivermectin was discovered in 1975 and commercially commercialised in 1981 for parasitic infection purposes in livestock before being authorised for clinical usage in 1987 for treatment of Lyme disease and a variety of human parasitic infestations, including river filariasis, strongyloidiasis, and parasitic organisms that cause, rosacea, pediculosis, and scabies.[1,5]

Ivermectin has the unique property of being adapted pharmacodynamically by changing the kind of formulation.[6] The medium employed in Ivermectin drug formulations has critical control over its uptake from the site of injection and, as a result, bio-accessibility.[7] Several findings have emerged since 2012, suggesting that Ivermectin has antimicrobial activity[8–12] against an increasing variety of RNA viruses, such as HIV-1, dengue virus, Zika virus, influenza, and more importantly COVID-19.[11,56,57] Pseudorabies, polyoma, and adenoviruses are among the DNA viruses that have been shown to be responsive to Ivermectin.[13,14] Furthermore, Ivermectin has lately acquired popularity as a

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List of abbreviations

COVID-19	Coronavirus Disease 2019
HIV	Human Immunodeficiency Virus
LMICs	Low- and Middle-Income Countries
FDA	Food and Drug Administration

novel approach to preventing transmission of malaria. It focuses mostly on the zoophagic characteristic of the vector that transmits the disease, Anopheles mosquito.[3,15] Moreover, Ivermectin therapy to animals has been proven to effectively prevent malaria transmission to humans from mosquitoes.[3,15] Interestingly, the interaction with and blockage of the host importin (IMP) protein is the foundation of Ivermectin's broad-spectrum antimicrobial action.[10,13,14] Although Ivermectin is believed to facilitate nuclear importation of several virus particles and critical host components, additional antimicrobial effects were postulated,[16] notably when it comes to COVID-19.[17]

Ivermectin's therapeutic efficacy against SARS-CoV-2 has been investigated by Caly et al.[11] The researchers showed that a single dosage of Ivermectin reduced SARS-CoV-2 multiplication in Vero/hSLAM cells by about 5000-fold. This discovery has piqued the curiosity of scientists and healthcare professionals across the globe.[18] Nevertheless, the findings should indeed be viewed with utmost care,[18] and its usage, particularly in severely ill people, necessitates rigorous risk–benefit analysis.[19] To begin with, Ivermectin was only evaluated in vitro, which used a single line of monkey kidney cells that were modified to produce signalling lymphocytic activation molecule (SLAM) of humans, commonly referred to as CDw150 (a measles virus receptor).[20] According to existing research, substantial levels of Ivermectin action towards SARS-CoV-2 will need drastic, perhaps lethal, increases in Ivermectin dosages in people.[21] Not surprisingly, it has been suggested that before using Ivermectin to cure SARS-CoV-2, excellent research studies guided by rigorous pharmacokinetic designs must be investigated to confirm its effects.[21] Nonetheless, findings using laboratory animals indicating up to about 3-fold increasing levels in the respiratory tract than in plasma 1 week after mouth dosage suggests that more study is needed, especially for treating certain types of viral infections.[22]

Since finding new treatments takes a long time, discovering existing drugs that could be repurposed for COVID-19 and have proven safety and efficacy characteristics based on decades of usage might be important in reducing or perhaps eliminating the COVID-19 pandemic.[23] This is particularly important as many of the global population, particularly amongst low- and middle-income countries (LMICs), may take months, if not years, to get vaccinated, using repurposed drugs may be imperative.[23] Interestingly, the blocking of importin α/βmediated nuclear import of virus particles is postulated as the likely process behind Ivermectin's antivirus potential, given its ability to suppress viral multiplication.[24] Because SARSCoV-2 is an RNA virus, it could have an identical potency.[25] Ivermectin is also being suggested to play an ionophore function.[26] As ionophore compound is being characterized as a possible antiviral therapeutic,[11] Ivermectin might eventually cause an ionic disequilibrium, compromising both structure and functioning of the SARSCoV-2 membrane.[18]

Ivermectin is presently commercially accessible and cheap in several places across the World.[24] As per a 2018 petition for Ivermectin usage against scabies, the expense of a hundred 12-mg pills is 2.90USD. Hence, investigating Ivermectin's therapeutic role towards SARS-CoV-2 might be very important for resource-constrained environments.[27] If proven successful as a COVID-19 therapy, its economic feasibility ought to be weighed based on the cost of available therapeutics and prophylaxes. This paper aims to review the effectiveness of Ivermectin as a therapy for COVID-19 infection.

2. Mechanism of action of Ivermectin

Research by Gupta et al.[28] suggest that Ivermectin is an anti-helminthic agent that causes hyperpolarization of GABA-gated Cl channels, resulting in the paralysis of the infected organism. Immunomodulation of the host response has also been proposed as a mechanism with the same effect. This is accomplished through neutrophil activation and an increase in C-reactive protein levels and interleukin-6. According to Njoo et al.[29] Ivermectin's antiviral activity has just been recently identified. It has satisfactorily shown to be effective against several flaviviruses in vitro. These flaviviruses include (dengue fever, Japanese encephalitis, and tick-borne encephalitis virus) as well as the chikungunya virus. Mastrangelo et al.[16] and Varghese[12] also confirm that the same activity has been tested in various viral illnesses in their studies. Its effectiveness in killing or eradicating coronavirus in vitro has recently been discovered. The particular mechanism responsible for this action has yet to be determined, although it is thought to be through the suppression of importin α/β1 mediated trafficking of viral proteins into and out of the nucleus. Importins are a type of karyopherins. The speculated inhibitory action of Ivermectin on importin α/β mediated transport system, based on this hypothesis, suggest a possible role of Ivermectin in the elimination of COVID-19.[30] Caly et al.[11] looked for viral RNA levels in the Vero/hSLAM cells (Supernatant and cell pellets) that had been infected with SARS-CoV-2 (isolate Australia/VIC01/2020) and then treated with 5 μM Ivermectin 2 h later. They noticed a 93% and 98% decrease in viral load after 24 h. At 48 h, a further reduction (~5000 fold) in the viral RNA load only was noted. With this research, the investigators could comment on the inhibitory concentration 50 (IC50), which was estimated to be ~2 Mm.[11] In another study, it was documented that no toxicities were found for the concentrations at which Ivermectin was tested.[28] In vivo, however, the required cell culture EC50 may not be practical. Schmith et al.[31] said that among other hypothesized mechanisms is the Inhibition of SARS-CoV-2 3CLPro activity (a protease required for viral replication). Another researcher suggests that the drug acts through various anti-inflammatory effects.[32] Another suggested mechanism is the competitive binding of Ivermectin with the viral S protein, as shown in many silico studies.[33,34] The latter would prevent the virus from attaching to ACE-2 receptors, suppressing the infection.

Hemagglutination via viral binding to sialic acid receptors on erythrocytes is another proposed pathologic mechanism that would be similarly disrupted. Although, both host-directed and virus-directed mechanisms have thus been proposed, the clinical mechanism may be multimodal, possibly dependent on the disease stage, and a comprehensive review of mechanisms of action is warranted.[23]

The in vitro potency of Ivermectin against COVID-19 virus suggests a great potential for the drug to be utilized in the management of SARS-CoV-2 infection. However, the conditions in which the virus replicates and infects the cells in vivo and in vitro differs, this makes a definitive conclusion on its benefit in patient care that cannot be made yet. Ivermectin proves to be more effective in treating COVID-19 than other drugs, for example, the adverse effects associated with hydroxychloroquine (irreversible retinal damage, prolong QT interval, myopathy, neuropathy) or with lopinavir + ritonavir combination (hypertriglyceridemia, hypercholesterolemia) are not seen in patients who are on Ivermectin.[35,36] Furthermore, the treatment regime with Ivermectin may turn out to be more cost-effective. This may create an apparent shortage of this drug, a standard treatment for patients with auto-immune diseases. Considering all these, one can conclude that clinical trials with Ivermectin should be conducted in COVID-19 patients to detect if the drug can positively affect treating patients that already have complications because of the infection.

3. Uncertainty about the clinical efficacy of Ivermectin in the management of COVID-19 infection

As the world continues to grapple with COVID-19 pandemic, research interest continues to target preventive and treatment options available to alleviate or minimize the health challenges associated with the infection. Apart from preventive measures, drugs like remdesivir, corticosteroids, antioxidants, and azithromycin have been utilized in various combinations to manage the different presentations of COVID-19 infections. Remdesivir seems to be one of the few drugs that have found to be useful in treating infected patients. The role of some other drugs like hydroxychloroquine, chloroquine and Ivermectin has been controversial. Recent studies focus on the clinical usefulness of Ivermectin as a preventive and treatment option in curbing the disease, especially in countries with low and medium income.

Although some in-vitro studies have documented its activity against viruses like Zika, dengue, human immunodeficiency virus (HIV) and yellow fever, in-vivo studies are still few, so the data available is inconclusive for its recommendation or approval as an antiviral in humans. Since the reported activity of ivermectin against SARS-CoV-2 in the in-vitro study,[11,56,57,60] reports from other researchers suggest a possible role for ivermectin in minimising the spread of COVID-19. Evidence from randomized trials has been conflicting. While some studies found some degree of efficacy, others documented no benefits. Lopez-Mendez et al.,[37] following a randomized trial, reported its ineffectiveness in providing improvement in mild cases. The meta-analysis by Bryant et al.,[23] assessed the ability of ivermectin to prevent infection of healthcare workers and those in contact with people already infected with the virus. The result of their study showed that ivermectin was able to prevent infection in more than two-thirds of the participants [86% (79%–91%] (In 3 trials, 738 participants aRR 0.14, 95% CI 0.09–0.21; 5.0% vs. 29.6% contracted COVID-19, respectively). The findings from their study also suggested that Ivermectin has survival benefit as it was observed to decrease the rate at which the disease worsen especially if treatment was commenced early, and reduce the risk of death by 62% (95% CI 27–81%) with average RR (aRR- 0.38, 95% CI 0.19–0.73; I2 = 49%). They concluded that early use might have a place in the reduction of morbidity and mortality. A real-time meta--analysis[38] of available data on Ivermectin in COVID-19, reveals a 79% (RR 0.18 [0.11–0.31]) and 85% (0.12[0.05–0.30]) improvement in patients who had early treatment and prophylaxis respectively. There were reduced numbers of those who died, those who required intensive care, the number of days spent as in-patients and increased viral clearance. They were convinced that the effects observed were not a chance finding.[38] Their conclusion was similar to that documented by Pierre et al.[39] In another meta-analysis, Roman et al.[40] did not observe any of the positive effects of Ivermectin reported by other researchers. They concluded that the drug was not a viable option for the disease. In another study, Behera et al.[41] reported a 73% reduction in viral load when 300 μg/kg of Ivermectin given as a two-dose regimen 72 h apart was used to prevent infection a healthcare worker. The reduction was observed after one month of use. They suggested that chemoprophylaxis with the drug may be employed as a stop-gap to curb the spread of the infection until a vaccine is widely available. Chosdow et al.,[42] expressed their concern about the pharmacokinetics and pharmacodynamics of the drug, which is only given as oral tablets in humans. Reconstituting the drug into a solution has been advised against owing to its poor solubility in aqua. Veterinary medicines use the oral solution form of the drug that is available for animals, and WHO has warned that this formulation should not be used in man.[43] WHO still recommends that owing to the lack of sufficient data, Ivermectin should only be used for research purposes or clinical trials.

4. Ivermectin products for animals versus Ivermectin products for humans

Ivermectin is a drug for humans and animals to treat internal and external parasites, including certain types of worms, fleas, ticks, and lice.[44] According to some research, Ivermectin products for animals are not intended for COVID-19 treatment.

Ivermectin for animals is available in five forms: injectable, oral liquid, powder, pour-on, and pills, with the most prevalent injectable form. Ivermectin for humans is available in pill or tablet form. Animal Ivermectin may, however, be harmful to humans. Ivermectin overdose can have serious repercussions for the human brain and vision. The Food and Drug Administration (FDA) is responsible for protecting public health by ensuring the safety and efficacy of human and veterinary drugs. In their 2018 write up, the FDA outlined that in humans, Ivermectin tablets are FDA-approved for treating some parasitic worms. In addition, some topical formulations are FDA-approved for the treatment of external parasites, for example, head lice and skin conditions such as rosacea. In animals, Ivermectin is FDA-approved for the prevention of heartworm disease in dogs and cats and for treating certain internal and external parasites in livestock.[44]

The FDA has not reviewed sufficient data to support Ivermectin in COVID-19 patients to treat or prevent COVID-19. More research is still being constructed. Therefore, we cannot rule out the use of Ivermectin or consider it unapproved. It is important to be cautious as certain levels of Ivermectin for approved uses can interact with other medications, like anticoagulants. Another fact to note is that Ivermectin can be overdosed, which can cause nausea, vomiting, diarrhoea, hypotension (low blood pressure), allergic reactions (itching and hives), dizziness, ataxia (problems with balance), seizures, coma, and even death.

In veterinary medicine, many medications are regularly administered for off-label use. Ivermectin can be used with other deworming drugs. Ivermectin comes in a variety of forms, including tablets, chewable tablets, topical liquid (for ear mite treatments), and an injectable. It's possible to take it with or without food. The drug is given to animals with food or a smear if they vomit or act sick after receiving it. However, some Ivermectin side effects may not be detected visibly, necessitating laboratory testing to determine the drug's effectiveness.[45]

Animal medications are sometimes highly concentrated because they are intended for huge animals such as horses and cows, weighing more than humans. In humans, such high doses can be extremely hazardous. The FDA examines medications not just for the active ingredients' safety and effectiveness but also for that the inactive ingredients. In animal products, there are many inactive substances that have not been tested for human use or are present in far higher quantities than those used in people. It is unclear how these inactive substances will affect Ivermectin absorption in the FDA's human body.[50] Therefore Ivermectin drugs should not at all be used in humans, and messages of caution must be clearly communicated to the public and advise them to completely desist from taking Ivermectin medications intended for animal use.[51]

5. Ongoing clinical trials

As of the 17.05.2022, there are 102 clinical trials[58] that study the potential use of Ivermectin in the treatment of COVID-19. Within the African continent, the University of Zagazig in Egypt[46–49] studied Ivermectin as a prophylactic option in asymptomatic family contacts for patients with COVID-19. Out of these studies, we identified seven completed studies, as indicated in Table 1 below.

6. Real-time meta-analysis of the use of Ivermectin for treating COVID-19

A real-time meta-analysis study[38] has reported 63% and 83% improvement for early treatment and prophylaxis (RR 0.37 [0.28–0.47] and 0.17 [0.11–0.26]) respectively.[59] In addition to randomized clinical

Table 1
Ongoing clinical trials to study the potential use of Ivermectin to treat COVID-19.

Title of the Study	Medications used	Location of the Study
Effectiveness of Ivermectin as add-on Therapy in COVID-19 Management	Ivermectin	General Directorate of Medical City, Bagdad, Baghdad, Iraq
USEFULNESS of Topic Ivermectin and Carrageenan to Prevent Contagion of Covid 19	A combination of Iota carrageenan nasal spray and Ivermectin oral drops (used as buccal drops)	Hospital Eurnekian, Buenos Aires, Argentina
Prophylactic Ivermectin in COVID-19 Contacts	Ivermectin Tablets	Zagazig University, Zagazig, Sharkia, Egypt
Clinical Trial of Ivermectin Plus Doxycycline for the Treatment of Confirmed COVID-19 Infection	Ivermectin and Doxycycline Drug: Standard of care	Dhaka Medical College, Dhaka, Bangladesh
Sars-CoV-2/COVID-19 Ivermectin Navarra-ISGlobal Trial	Ivermectin Drug: Placebo	Clinica Universidad de Navarra, Pamplona, Navarra, Spain
Ivermectin, Aspirin, Dexamethasone and Enoxaparin as Treatment of Covid 19	Ivermectin 5 MG/ML oral solution, Aspirin 250 mg tablets|Other: Ivermectin 5 mg/mL oral solution, Dexamethasone 4-mg injection, Aspirin 250 mg tablets Other: Ivermectin 5 MG/ML oral solution, Dexamethasone 4-mg injection, Enoxaparin injection. Inpatient treatment with mechanical ventilation in ICU.	Hospital Eurnekian, Buenos Aires, Argentina
Efficacy, Safety and Tolerability of Ivermectin in Subjects Infected With SARS-CoV-2 With or Without Symptoms	Ivermectin drug: Placebo	Investigación Biomédica para el Desarrollo de Fármacos S.A. de C.V., Zapopan, Jalisco, Mexico
Ivermectin for Severe COVID-19 Management	Ivermectin	Afyonkarahisar Health Science University, Afyonkarahisar, Turkey, Gulhane Faculty of Medicine, University of Health Sciences, Ankara, Turkey Ankara City Hospital, Ankara, Turkey Haydarpasa Sultan Abdulhamid Han Training and Research Hospital, Instanbul, Turkey

studies, either in-vitro or conclusive evidence or observational studies are being carried out to investigate and find an effective and safe antiviral treatment for COVID-19. Although there are mixed results on the use of Ivermectin to treat COVID-19, a recent paper that investigated the prevention and treatment of COVID-19 infection concluded that there is evidence with moderate certainty showing a large reduction in COVID-19 deaths is possible with Ivermectin.[27,52] Fig. 1 below indicates a list of 45 out of 82 Ivermectin COVID 19 randomized clinical trials.

7. Comparison of COVID-19 cases before and after the administration of Ivermectin

Recent studies on Ivermectin have illustrated the antiviral role of Ivermectin and preliminary results from recent experimental reports highlighted an in vitro capability of withholding SARS-CoV-2 replication. As displayed in Table 2 above, about 81.8% of the Randomized Controlled Trials, including late treatment, showed positive results when Ivermectin was administered with a reduced risk of 0.44 and p-value less than 0.0001. On the other hand, 81.8% of the Randomiyed Controlled trials excluding late treatments showed a reduced risk RR of 0.33 also with a p-value less than 0.0001. The map below illustrates the adoption of Ivermectin in different countries across the globe. Currently, Ivermectin is used in about 44% of the World's Countries where COVID-19 mortality is close to zero were excluded because they may not have an incentive to adopt treatments.[1] This shows that Ivermectin has been adopted by approximately 28% of the World's population. South Africa, Zimbabwe, Nigeria and Egypt are the only African countries that have started to adopt the use of Ivermectin for COVID-19. In Europe, the first countries to adopt Ivermectin are Germany, Ukraine, Portugal and Slovakia. A large proportion of South American countries have also rolled out the use of Ivermectin for COVID-19, as shown in Fig. 2 below.

In the following subsections, we take Peru and South Africa as two case study countries that have begun the administration of Ivermectin, and we study the motivations and legal instruments put in place to commence the use of Ivermectin, patterns and trends of COVID-19 cases upon administration.

7.1. The case of Peru

The government of Peru started the administration and use of Ivermectin by decree on May 8, 2020.[40,53] This approval was based on the in vitro study conducted by Caly et al. from Australia.[11,41] Fig. 3 below shows how the Ivermectin intervention have matched with variations in the COVID-19 death rates in Peru. The figure indicates a decreasing trend in the 7 day average of COVID-19 infections per 100,000 and a reduction in the 7 day average of total deaths per 100,000. This being the case, there are no documented randomized clinical studies to prove the clinical efficacy of Ivermectin in Peru.

7.2. The case of South Africa

The South African Health Products Regulatory Authority (hereafter abbreviated as SAHPRA) approved the controlled use of Ivermectin for humans in January 2021. In principle, there are two legal ways by which Ivermectin can be prescribed for the treatment of COVID-19:

- ***Ivermectin controlled compassionate use programme:*** Ivermectin can be used as covered under Section 21 of the Medicines and Related Substances Act, relating to prescribing Ivermectin in the management of COVID-19.[54]
- ***Patient basis approval:*** Under Section 14 of the South African Medicines Act, once a drug has been registered for human use in South Africa, it is possible for a doctor to make a prescription to be taken to a compounding pharmacy, which will compound and dispense Ivermectin for COVID treatment.[54]

Although[55] reports that the number of new COVID-19 infections in South Africa has been declining since the controlled use of Ivermectin was permitted by SAHPRA, we are of the view that comprehensive clinical trials should be carried out to determine the impact and clinical efficacy of the use of Ivermectin on infection rates, and mortality in South Africa.

8. Conclusions

The aim of this paper was to investigate scientific literature which supports the existence or nonexistence of a link between the administration of Ivermectin and a reduction in COVID-19 death rates and improvement in recovery rates. Currently, the Food and drug administration (FDA) has not approved any specific treatment or drug available

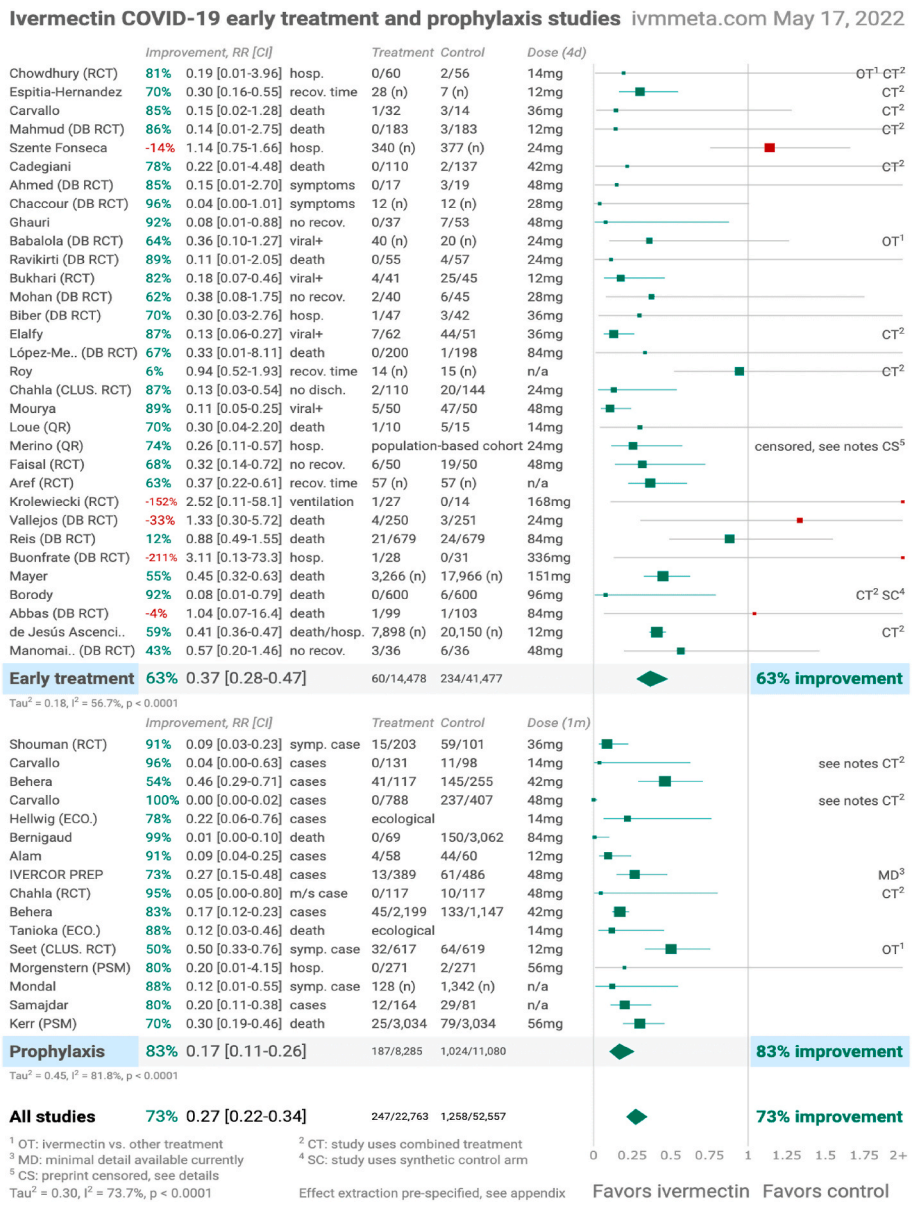

Fig. 1. Analysis of studies concerning the use of ivermectin for the treatment of COVID-19.
Source: https://ivmmeta.com/

Table 2
Summary of the randomized controlled trials.

Treatment Time	Number of Studies reporting positive effects	Total number of studies	Percentage of studies reporting positive effects	Probability of an equal or greater percentage of positive results from an ineffective treatment	Random effects meta-analysis
Randomized Controlled Trials	27	33	81.8%	1 in 6 thousand	56% improvement RR 0.44 [0.32–0.61] p < 0000.1
Randomized Controlled Trials (excluding late treatment)	18	22	81.8%	1 in 460	67% improvement RR 0.33 [0.21–50.51] p < 0.0001

or under testing for COVID-19, which is deemed to be clinically effective. Supportive symptomatic treatment remains at the core of COVID-19 therapy.

We found out that there are inconclusive results on the potential use of ivermectin in the treatment of COVID-19. Whilst some studies have reported that ivermectin might have a prophylactic effect against SARS-CoV-2, other meta-analysis studies have argued that treating SARS-CoV-2 with ivermectin does not result in lower hospitalization rates or extended observations in intensive care units. This unclear efficacy of ivermectin necessitates well-designed randomized clinical trials to study the clinical efficacy of Ivermectin and its potential application and administration. Furthermore, researchers posit that there is a need to put

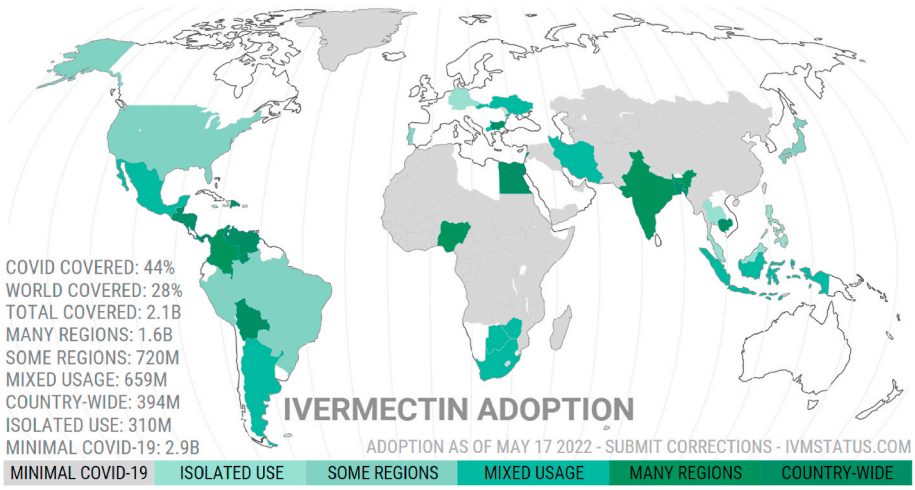

Fig. 2. Map showing the adoption of Ivermectin for COVID-19 treatment in the world.
Source: Global Ivermectin adoption for COVID-19: 44% (ivmstatus.com)

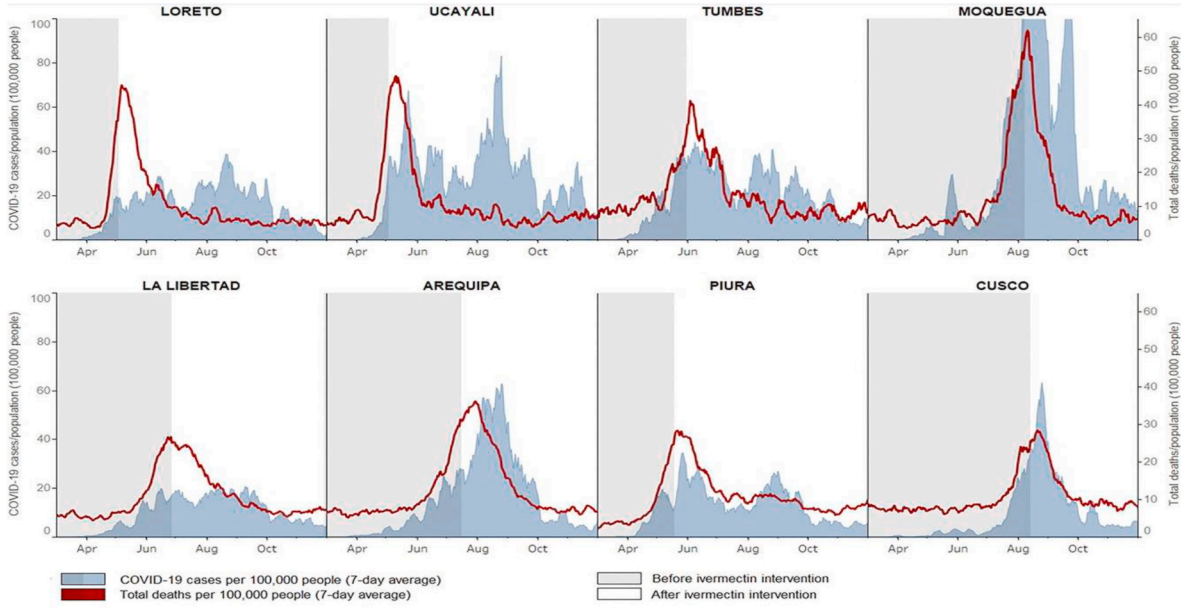

Fig. 3. COVID-19 cases in Peru prior and post-administration of Ivermectin.
Source*: Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19. [75]*

regulatory control measures in place to guide diligent testing of Ivermectin before its establishment as a treatment against SARS-CoV-2.

The continued fragilities of health care systems in especially developing countries' challenges would be greatly eased if more updated and evidence-based research on potential COVID-19 treatments and guidance came from leading health care institutions. We reiterate that, even with the real-time meta-analysis study cited in this paper, there is currently no 100% effective drug or medication for all current variants of COVID-19. And more controlled clinical trials should be carried out to fully explore the possibility of using Ivermectin for COVID-19, and countries must continue to endeavour to share the responsibility of curbing and risk this pandemic from taking more lives.

Author contribution

Conceptualization (HO, PT), first draft (HO,PT, JC, OM, OU), Editing (HO, PJ, JC OM and OU).

Ethical considerations

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Data availability

Derived data supporting the findings of this study are available from the corresponding author on request. The data that support the results of

this study are available on request from the corresponding author.

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