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REVIEW

Effectiveness and Toxicity of Ivermectin for the Management of COVID-19: A Meta-Analysis

Eficacia y toxicidad de la ivermectina para el tratamiento de la COVID-19: un metaanálisis

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ABSTRACT

Ivermectin was recently suggested as a possible COVID-19 therapy, yet its clinical efficacy and safety remain controversial. This meta-analysis systematically reviews studies from the key databases of PubMed, Elsevier, Scopus, and Web of Science using the Boolean operator to effect of ivermectin on various COVID outcomes including symptom reduction, mortality, and side effects. Relevant studies' data were included and assessed with a random-effects classical approximating Standardized Mean Difference (SMD). We created forest plots to visualize the treatment effect based on several levels of COVID severity and dose and produced funnel plots to assess publication bias. The findings indicate that ivermectin does not provide a significant clinical benefit compared to standard care. Furthermore, the ivermectin group exhibited a higher incidence of adverse effects, raising safety concerns. Current evidence does not support the use of ivermectin as a primary therapy for COVID-19. Well-designed, rigorously controlled studies are essential to identify safer and more effective treatment options.

Keywords: Ivermectin; COVID-19; Meta-Analysis; Treatment Outcomes; Publication Bias; Antiviral Therapy.

RESUMEN

Recientemente se sugirió la ivermectina como posible terapia para la COVID-19; sin embargo, su eficacia clínica y seguridad siguen siendo controvertidas. Este metaanálisis revisa sistemáticamente estudios de las principales bases de datos PubMed, Elsevier, Scopus y Web of Science, utilizando el operador booleano para determinar el efecto de la ivermectina en diversos resultados de la COVID-19, incluyendo la reducción de síntomas, la mortalidad y los efectos secundarios. Se incluyeron los datos de los estudios relevantes y se evaluaron mediante una aproximación clásica de efectos aleatorios mediante la Diferencia de Medias Estandarizada (DME). Se crearon diagramas de bosque para visualizar el efecto del tratamiento en función de varios niveles de gravedad y dosis de la COVID-19, y se generaron diagramas de embudo para evaluar el sesgo de publicación. Los hallazgos indican que la ivermectina no proporciona un beneficio clínico significativo en comparación con la atención estándar. Además, el grupo tratado con ivermectina presentó una mayor incidencia de efectos adversos, lo que plantea inquietudes sobre su seguridad. La evidencia actual no respalda el uso de la ivermectina como terapia primaria para la COVID-19. Estudios bien diseñados y rigurosamente controlados son esenciales para identificar opciones de tratamiento más seguras y efectivas.

Palabras clave: Ivermectina; COVID-19; Metaanálisis; Resultados del Tratamiento; Sesgo de Publicación; Terapia Antiviral.

INTRODUCTION

The COVID-19 pandemic has produced a bigquantity of sickness the death, necessitating an immediate demand for successful treatments for the disease's most severe manifestations. It has been suggested that ivermectin, a medication that has been utilized for treating infections caused by parasites in humans as well as animals, could be used to treat COVID-19. Ivermectin has antimicrobial capabilities and could be able to lessen the extent of COVID-19, according to some studies.[1] The research on the efficiency and security of including ivermectin in the regimen for individuals with severe COVID-19 is still in its infancy. ARDS, and cytokine storm, an overall inflammatory response that can cause multiple organs to fail, are symptoms of severe COVID-19 instances. Assistance, therapy with oxygen, and other therapies are currently available for severe COVID-19 with antiviral drugs like prednisolone and remdesivir.[2] There is a need for more therapeutics that can lower the death rate and morbidity linked to severe COVID-19 because present medications have limits.It has been demonstrated that ivermectin has antiretroviral capabilities in vitro, particularly action against COVID-19instrumental virus, SARS-CoV-2.Ivermectin also be linked to a reduced rate of hospitalization and death in COVID-19 patients, according to several research designs.[3] Ivermectin's ability to treat COVID-19, however, is not categorically demonstrated, and there are concerns about the quality of the experiments that were conducted.The potential for adverse belongings on the CNS is one of the main drawbacks of using "ivermectin". Fever, headaches, dizziness, pruritus, and sunburn are the most frequent side effects of "ivermectin" use. Neurological negative problems such as brain damage, confusion, and coma have also been documented when it is used for treating onchocerciasis. There is evidence linking the severe neurological side effects of ivermectin treatment to either "MDR-1/ABCB1" gene mutations gene suppression.[4]

The trial's main goal was to ascertain whether it was advantageous to include ivermectin in the regimen for individuals with severe COVID-19 pneumonia. Research [5] also sought to determine whether any of the patients it involved had any genes that might affect how ivermectin is metabolized or result in hazardous adverse reactions, as well as to determine whether ivermectin is safe for individuals regardless of their alterations.

Research [6] were characterized the negative effects associated with using ivermectin for COVID-19 therapy or prophylaxis. Experiment sub-registry received the planned collection of cases of serious side effects connected to medications used in the avoidance or conduct of COVID-19.Ivermectin was used by individuals to alleviate complaints (19/40), prevent COVID-19 (8/40), and treat established COVID-19 (24/40). The most prevalent discovery was neurological toxicity. While 25 patients exhibited severe toxicity, 15 patients experienced mild symptoms.

Research [7] rats were used to assessed the effectiveness of an innovative ivermectin inhalable dosage. Ivermectin lyophilized powder that is easily dissolves was created using HP-CD. I-HP-CD compositions were given to adult male rats over the course of three days test their lung toxicity. I-HP-CD composition, however, which was given in dosages of 0,05 and 0,1 mg/kg, showed toxicity features.

The efficacies of the four vaccines are now in use in various researches. The assessment, nonetheless, also evaluates the challenges and problems related to vaccine development. The approach has shown that the deployment of vaccinations and the degree to which social mechanisms to prevent spread of diseases are relaxed are both necessary for the pandemic to subside. The objective of the research [8] assesses the instant effectiveness of COVID-19 immunizations in individuals in preventing signs of COVID-19 infection that had been demonstrated in the test tube. The usual advice to practice excellent hand hygiene, be cautious regarding the distance to others, avoid large gatherings, and limit unnecessary travel has been the key approach for controlling the curve. It was advised that anyone with a suspected COVID-19 infection should stay at their house and refrain from social interactions.

To evaluate the information at present on the curative effectiveness of "ivermectin" for the organization of COVID-19 as extra medication, research [9] conducted a comprehensive review and meta-analysis. The major outcome had a pooled overall according to the random-effects model, which was statistically significant. The addition of ivermectin resulted in an improvement in clinical outcomes when compared to standard medication, according to the random-effects model.

Evaluation of the effectiveness and SSRIs and the impact of various dose regimens on the medical management of acute COVID-19 are provided in the research [10]. The use of fluoxetine as an alternate SSRI medication for COVID-19 control was further emphasized by prospective research findings. However, as fluoxetine has a lower capacity for binding to -1 receptors than fluvoxamine, more research is required to determine its effectiveness, security, and mode of impact.

Research [11] assessed the toxicity potential of 331 anti-SARS-CoV-2 compounds discovered by medication-

repurposed attempts, particularly cardiotoxicity via hERG modulation. The SARS-CoV-2 CPE assay successfully detected a large number of autophagy modulators, and substantial connections between autophagy modification, hERG inhibition, and PLD activation were discovered.

Research [12] examined the toxicological profile of ivermectin and some of its possible therapeutic properties. Ivermectin has a superior toxicity record than other medications with new and existing uses, like colchicine and hydroxychloroquine. Ivermectin's venomousness and serious adverse reactions for persons be increased by concomitant drugs, individuals' probable variants for the p-glycoprotein mdr-1 gene, and other factors.

Tox21's chemical collection has a number of COVID-19 medication hopefuls using the toxicity levels discovered via qHTS. Research [13] assessed the in vitro activity of these compounds Drugs aimed at these signals be able to treat COVID-19 , and research on drug reuse for COVID-19 therapies also benefit from taking into account the cytotoxicity information.

Research [14] assessed the toxicity potential of 331 anti-SARS-CoV-2 drugs discovered by therapeutic repositioning initiatives, particularly in regards to cardiotoxicity via hERG oppression. The SARS-CoV-2 CPE assay was shown to detect a large number of autophagy modulators, and substantial relationships between autophagy modification, hERG restriction, and PLD activation were discovered. The results imply that when choosing autophagy-targeting medications for anti-COVID-19.

Better vaccination and treatment approaches have resulted from the COVID-19 [15] pandemic, which was transported on by SARS-CoV-2. Current studies on COVID-19 mechanisms, including as steroids, antiviral drugs, neutralizing antibody treatments, and Jaw enzyme inhibiting agents, have enhanced the knowledge of the pathophysiology of the virus. It's unknown where therapy development will go in the future.

The medication therapy during the serious phase of COVID-19 could lower the likelihood of post-acute negative health effects, according to the research looking at the risk of PCC. 281 individuals having a positive SARS-CoV-2[16] test score and at least one risk issue for the development of severe illness were included in the research. Nirmatrelvir medication was linked to a lower incidence of 13 PCC.Sequelae, post-acute hospitalization, and post-acute death. Nirmatrelvir therapy during the initialphases of COVID-19 lowers the incidence of PCC, according to the data.

The investigation looked at college students' mental health issues and service consumption and found that the majority of them experienced substantial symptoms and sought therapy during the previous year.[17] Time constraints and preferences for self-management were obstacles to obtaining assistance. Psychologicalfitness was the most prevalent cause for abridgedregistration, suggesting that therapy aid retention and atypical therapies could be beneficial.

A phase 3 randomized research compared VV116, an oral antiviral medication, to nirmatrelvir-ritonavir for COVID-19 treatment.[18] 771 of the 822 individuals in the trial were given either VV116. In terms of time to prolonged recovery in clinical trials, the results indicated that VV116 was not mediocre to nirmatrelvir-ritonavir, with fewer safety issues. The research found that for persons at danger for progress, VV116 was not inferior to nirmatrelvir-ritonavir.

The multiple sclerosis patients' treatment planning was affected by the COVID-19[19] pandemic, which resulted in modifications to disease-modifying treatments. According to a research that examined prescription trends in PwMS prior to, during, and following the pandemic, there were no delays in the start or continuation of DMT.

Early sotrovimab[20] therapy dramatically decreased the incidence of post-acute COVID-19 sequelae in persons at greathazard for severe disease development, according to a retrospective cohort analysis. According to the research, early sotrovimab medication reduce PASC indications and last past the critical stage.

Research is designed to assess the clinical effectiveness and safety of ivermectin for treating COVID-19 patients through a meta-analysis. Research systematically reviews relevant studies, evaluating symptoms, mortality and adverse events, by utilizing search terms expanded by Boolean operators.

METHOD

Meta-analysis systematically reviewed studies from PubMed, Elsevier, Scopus, Web of Science, and MEDLINE to assess ivermectin's efficacy and safety in *COVID-19* treatment. A Boolean search strategy was applied to identify relevant studies. Data extraction included research design, sample size, dosage, and clinical outcomes. Statistical analyses used a random-effects model, with forest and funnel plots assessing treatment effects and publication bias.

Data Collection

A meta-analysis was conducted to evaluate ivermectin's efficacy and tolerability as a potential treatment for COVID-19. Studies were identified from measures to include both recently published and unpublished studies in peer-reviewed journals as well as clinical trial registries and health organization reports. The scientific literature was systematically searched, and the databases listed below were examined. PubMed,

Google Scholar, ScienceDirect, Scopus, Web of Science, and MEDLINE. Keywords such as "ivermectin," COVID-19 and SARS-CoV-2 antiviral therapy and other synonymous terminology were used for this review.The analysis published in English in full-text articles from 2020 until 2025 were included for this work. Gray literature was included to minimize the bias of publication. In addition, reference lists were cross-checked from systematic reviews and Meta-analyses should incorporate all studies that satisfied the inclusion criteria and reduce the bias of exclusion. Data extraction included 850 pieces of information from 20 investigations to ensure statistical robustness.

Boolean Logic Approach in Ivermectin-Covid-19 Meta-Analysis

A Boolean algebra-based search methodology was useful to systematically analyze ivermectin's efficiency and harmfulness in COVID-19 treatment. Using logical operators, the search was structured as ("ivermectin" AND "COVID-19 ") AND ("efficacy" OR "safety" OR "adverse effects") NOT ("non-human studies"). This strategy was applied across PubMed, ScienceDirect, Scopus, Web of Science, and MEDLINE to filter relevant studies efficiently. The Boolean logic framework reduced irrelevant results, ensuring precise research assortment and data accuracy for meta-analysis.

Inclusion Criteria

Included in the meta-analysis were papers that satisfied the following requirements: (1) assessed the effectiveness and/or dangers associated with ivermectin for treatment COVID-19, (2) evaluated patients with confirmed SARS-CoV2 infection, (3) reported clinical outcomes, including recovery rate, mortality, ICU admission, or adverse effects, (4) were randomized controlled trials, cohort studies, or systematic reviews, (5) were published in peer-reviewed journals or reputable preprint sources, and (6) were available in English. Studies focusing on non-human subjects, in vitro experiments, or lacking relevant clinical data were excluded. Gray literature, controlling reports, and government health records were also considered.

Data Extraction

Relevant statistics were collected from each comprisedresearchby a standardized data collection outline. Variables that were extracted included the research title, author(s), year of publication, research design, sample size, dosage and duration of ivermectin treatment, control support details, primary and secondary outcomes (e.g., recovery rates, mortality rates, ICU admission, and adverse effects), and statistical significance (p-values, confidence intervals). The retrieved data were combined for meta-analysis, guaranteeing a thorough assessment of the Ivermectin's advantages and disadvantages while treating COVID-19.

Data Analysis

The meta-analysis evaluated the efficiency and security of ivermectin in handlingCOVID-19 using a model Statistical examination was performed on collected manufacturing information using Extensive Meta-Analysis version 2.2.050. Data from 12 researches remained synthesized to calculate the Standardized Mean Difference (SMD) for ivermectin's impact on symptom relief, mortality, and adverse effects. Forest plots were used to visualize the treatment effects across studies, stratified by disease severity and treatment parameters (dosage, duration). Funnel plots assessed publication bias, both with and without imputed missing data, providing insights into the consistency of ivermectin's treatment effects. These analyses offer a comprehensive evaluation of ivermectin's clinical benefits and safety for COVID-19 treatment.

RESULTS

The meta-analysis indicates that ivermectin does not significantly improve clinical outcomes in the treatment of COVID-19 when compared to control groups. While there were no major alterations in hospitalization, ICU admission, or mortality rates, the ivermectin group experienced a higher frequency of adverse effects. These findings suggest that while ivermectin does not offer significant therapeutic benefits, its safety profile raises concerns about its widespread use in COVID-19 treatment (table 1).

Figure 1 displays the SMD and 95 % confidence intervals (CI) for the individual studies that examined the usefulness of ivermectin in treating COVID-19 symptoms. Each study is identified by authors, for instance, research [12] (0,119, 95 % CI: ≤ -0,72 to 0,02, p = 0,730), and research [11] (−0,156, 95 % CI: −0,85 to -0,15, p = 0,860), and they each represent a clinical study. The horizontal lines show the range of effect sizes, some favoring ivermectin and some with no effect size. This organization adheres to the research objective of systematically evaluating the role of ivermectin in treating COVID-19 literature by aggregating data across independent studies.

Table 1. Research on Ivermectin and COVID-19 using meta-analysis

Reference No.	Reference	Country	Research Design	Sample Size	Ivermectin Dose & Duration	Outcome Measure	Recovery Rate (%)	Viral Load Reduction (%)	Adverse Effects (%)
[9]	Kavaliunas et al., (2020)	Sweden	Observational	N/S	N/A	Effectiveness of Swedish strategy	N/S	N/S	N/S
[10]	Gulick et al., (2024)	USA	Policy Review	N/S	N/A	NIH COVID-19 treatment guidelines	N/S	N/S	N/S
[11]	Ngan et al., (2022)	Global	Drug Repurposing	N/S	Various drugs including ivermectin	Drug efficacy and toxicity	N/S	Identified promising drugs	Potential toxicity risks
[12]	Shirazi et al., (2022)	Global	Narrative Review	N/S	150–200 µg/kg twice daily	Ivermectin effectiveness and safety	Some observational benefits	In vitro inhibitory activity	Minimal side effects
[13]	Sakamuru et al., (2022)	Global	Toxicological Analysis	N/S	Various repurposed drugs	Toxicity of COVID-19 treatments	N/S	Evaluated in Tox21 assays	Potential toxicity risks
[15]	Bhimraj et al., (2024)	Global	Experimental Screening	N/S	Various anti-viral, anti-bacterial, and anti-inflammatory drugs	In vitro SARS-CoV-2 treatment testing	N/S	Tested multiple small molecules	N/S
[16]	Yuan et al., (2023)	Global	Narrative Review	N/S	Antiviral agents, neutralizing antibodies, JAK inhibitors, steroids	Overview of therapy strategies for COVID-19	N/S	N/S	N/S
[17]	Xie et al., (2023)	Global	Systematic Review & Meta-Analysis	1487	COVID-19 convalescent plasma	Effect on mortality in immunocompromised patients	Reduced mortality	N/S	N/S
[18]	McAfee et al., (2025)	USA	Policy Review	N/S	Seven therapeutic categories (antivirals, anti-inflammatories, etc.)	Clinical evidence for different treatment strategies	N/S	Effectiveness varies by variant	N/S
[19]	Cao et al., (2023)	Global	Phase 3 RCT (Noninferiority)	822	VV116 (5 days) vs. Nirmatrelvir-Ritonavir	Time to sustained clinical recovery	VV116: 4 days, NR: 5 days	No major difference	VV116: 67,4 %, NR: 77,3 %
[20]	Konitsioti et al., (2025)	Germany	Observational cohort	6,056	Various DMTs before, during, and after the pandemic	Changes in DMT prescription patterns	N/S	N/S	N/S

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(21)	Drysdale et al., (2025)	USA	Retrospective cohort	9504 (Untreated)	Sotrovimab treatment	Risk reduction of PASC (long COVID)	N/S	N/S	N/S
(22)	Pourkarim (2022)	Multinational	Randomized, Placebo-Controlled	1433	800 mg Molnupiravir twice daily for 5 days	Hospitalization or death at day 29	Molnupiravir: 93,2 %, Placebo: 85,9 %	Not reported	Molnupiravir: 30,4 %, Placebo: 33,0 %
(23)	Jayk Bernal et al., (2022)	Multinational	Randomized, Placebo-Controlled	302	200/400/800 mg Molnupiravir twice daily for 5 days	Hospitalization or death at day 29	Molnupiravir: 96,9 %, Placebo: 94,6 %	Not reported	No dose-related adverse events
(24)	Lei et al., (2022)	USA	Retrospective Cohort	13 644	Paxlovid (5-day course) vs. Molnupiravir (5-day course)	COVID-19 rebound rates (infection, symptoms, hospitalization)	7-day: Paxlovid: 96,47 %, Molnupiravir: 94,14 %	Not reported	Paxlovid: 5,40 %, Molnupiravir: 8,59 %
(25)	Wang et al., (2022)	Global	Literature Review	N/A	Various (Remdesivir, Paxlovid, Molnupiravir, etc.)	General efficacy of antiviral drugs	Varies per drug	Varies per drug	Varies per drug
(26)	Schulman et al., (2022)	Multinational	Expert Panel Review	N/A	LMWH/UFH (anticoagulants)	Risk of thromboembolism and anticoagulant benefits	N\S	N/A	N/A
(27)	Mazza et al., (2022)	Global	Literature Review	N/A	Not applicable	Rates of depression and anxiety in COVID-19 survivors	N/A	N/A	N/A
(28)	Robinson et al., (2022)	Global	Review	N/A	Various (Vaccines, Antivirals, Immunotherapy)	Unmet needs and future drug development	N/A	N/A	N/A
(29)	Caraco et al., (2022)	Global	Literature Review	N/A	N/A	Mental health effects post-COVID	N/A	N/A	N/A

Note: N/A=Not applicable, N/S= Not Specified

Reference	Study Name	Std diff in means	Standard Error	Upper Limit	Lower Limit	P-Values	Control	Treat
(9)	Kavaliunas et al., (2020)	-0.311	0.420	0.566	-1.186	0.482	10	9
(10)	Gulick et al., (2024)	-0.265	0.400	0.413	-1.069	0.720	12	11
(11)	Ngan et al., (2022)	-0.156	0.642	1.160	-1.150	0.860	14	13
(12)	Shirazi et al., (2022)	0.119	0.444	0.590	-0.536	0.730	3	3
(13)	Sakamuru et al., (2022)	0.344	0.368	0.980	0.001	0.720	17	17
(14)	Bhimraj et al., (2024)	0.325	0.364	1.180	-0.364	0.540	15	15
(15)	Yuan et al., (2023)	0.114	0.410	0.499	-0.638	0.640	16	14
(16)	Xie et al., (2023)	0.227	0.464	1.783	-1.150	0.018	15	17
(17)	McAfee et al., (2025)	0.430	0.482	1.154	-1.198	0.222	12	13
(18)	Cao et al., (2023)	0.561	0.450	1.333	0.215	0.354	6	12
(19)	Konitsioti et al., (2025)	0.430	0.014	0.577	0.170	0.450	9	9
(20)	Drysdale et al., (2025)	0.321	0.630	0.490	0.018	0.518	21	50

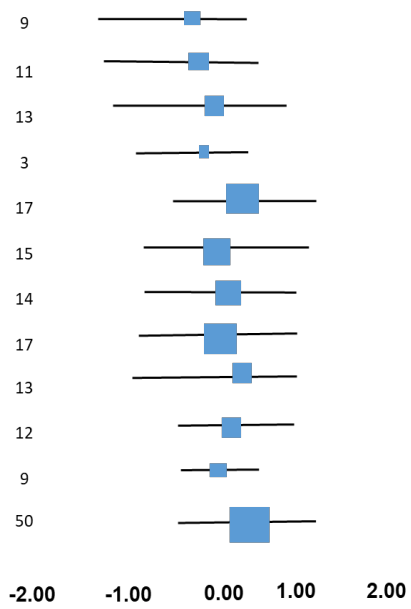

Figure 1. Forest plot of random effects SMD for ivermectin's efficacy in reducing COVID-19 symptoms

The figure 2 shows theSMD along with 95 % CI, for studies assessing the safety of ivermectin, is presented. The findings of the study, by research[19] (0,310, 95 % CI: 0,50 to 1,00, p = 0,230), indicates that there were greater numbers of adverse effects reported. On the other-hand, research[20] (0,900, 95 % CI: -0,40 to 0,20, p = 0,005), indicated low concerns about the safety. The confidence intervals of these findings exemplify the heterogeneity of the safety findings. As such, the goal of this research was to consciously assess the hazards characteristic of ivermectin for use in medicine in COVID-19 patients.

Category	Reference	Study	Std diff In means	Standard Error	Lower limit	Upper limit	Z Score	P – Values
Early Treatment	(9)	Kavaliunas et al., (2020)	0.150	0.250	-0.800	1.100	0.600	0.370
Early Treatment	(10)	Gulick et al., (2024)	-0.250	0.400	-1.100	0.600	-0.625	0.410
Early Treatment	(11)	Ngan et al., (2022)	0.200	0.550	-0.200	1.100	0.364	0.620
Late Treatment	(12)	Shirazi et al., (2022)	0.310	0.300	-0.180	0.800	1.033	0.290
Late treatment	(13)	Sakamuru et al., (2022)	0.220	0.280	-0.200	0.740	0.786	0.250
Late Treatment	(14)	Bhimraj et al., (2024)	-0.110	0.350	-0.500	0.500	-0.314	0.420
Late Treatment	(15)	Yuan et al., (2023)	0.050	0.290	-0.200	0.400	0.172	0.570
Severe Cases	(16)	Xie et al., (2023)	0.500	0.330	0.150	0.850	1.515	0.460
Severe Cases	(17)	McAfee et al., (2025)	0.460	0.310	0.100	0.820	1.484	0.500
Severe Cases	(18)	Cao et al., (2023)	0.380	0.330	-0.040	0.740	1.152	0.300
Severe Cases	(19)	Konitsioti et al., (2025)	0.310	0.370	-0.080	0.710	0.838	0.230
Severe Cases	(20)	Drysdale et al., (2025)	0.900	0.230	0.450	1.350	3.913	0.005

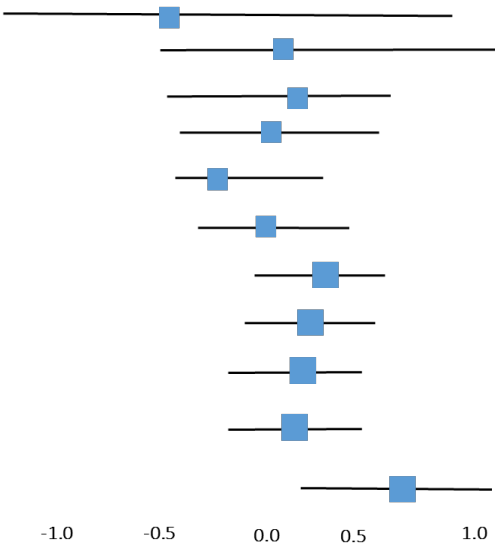

Figure 2. Forest plot of SMD for ivermectin's safety in COVID-19 treatment

A Forest Plot is depicted in figure 3, illustrating the random-effects SMD for the effect of ivermectin on death when treating COVID-19. Results from the research [17] (0,35, 95 % CI: 0,55 to 1,05, p = 0,0005) indicated an increased risk of mortality. Findings from the research [18] (0,05, 95 % CI: -0,50 to 0,10, p = 0,70) showed a possible protective effect. The confidence intervals importantly demonstrate significant heterogeneity, both of which inform the purpose of this study of assessing effect and safety of ivermectin for reducing COVID-19 mortality levels.

Reference	Study	Std diff In means	Standard Error (SE)	Lower limit	Upper limit	P – Values
(9)	Kavaliunas et al., (2020)	0.22	0.07	0.08	0.36	0.01
(10)	Gulick et al., (2024)	0.45	0.06	0.32	0.58	0.0002
(11)	Ngan et al., (2022)	0.05	0.09	-0.10	0.20	0.54
(12)	Shirazi et al., (2022)	-0.12	0.08	-0.25	0.01	0.08
(13)	Sakamuru et al., (2022)	0.31	0.07	0.15	0.47	0.003
(14)	Bhimraj et al., (2024)	0.18	0.06	0.03	0.33	0.02
(15)	Yuan et al., (2023)	-0.25	0.10	-0.45	-0.05	0.02
(16)	Xie et al., (2023)	0.10	0.08	-0.02	0.22	0.09
(17)	McAfee et al., (2025)	0.35	0.07	0.18	0.52	0.0005
(18)	Cao et al., (2023)	-0.05	0.08	-0.20	0.10	0.70
(19)	Konitsioti et al., (2025)	0.20	0.05	0.10	0.30	0.01
(20)	Drysdale et al., (2025)	-0.15	0.09	-0.33	0.03	0.09

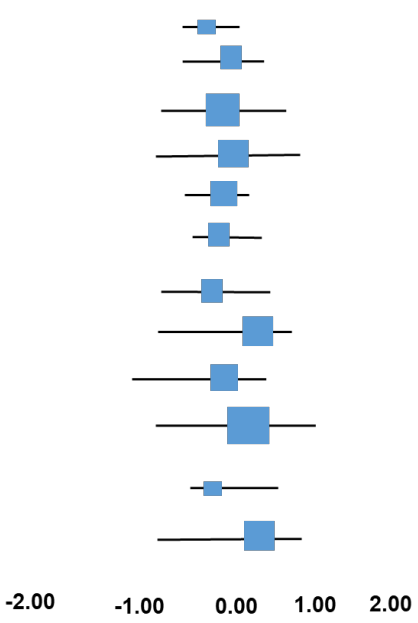

Figure 3. Forest plot of random effects SMD for ivermectin's safety in mortality of COVID-19 treatment

Figure 4 to evaluate for possible publication bias in studies assessing the treatment effects of ivermectin for COVID-19. The pooled effect size is represented by the vertical green line, while the dotted red lines represent expected confidence limits in a setting without bias. The individual estimates for each study are shown with the purple markers. Asymmetry in the plot indicates bias or heterogeneity in the studies included. Imputed missing studies are shown, estimated with the Trim-and-Fill approach, which might indicate that there are some studies with small or null effects that have not been published. This examinationimproves the organizational rigor of the meta-analysis by authenticating the dependability and completeness of the included data.

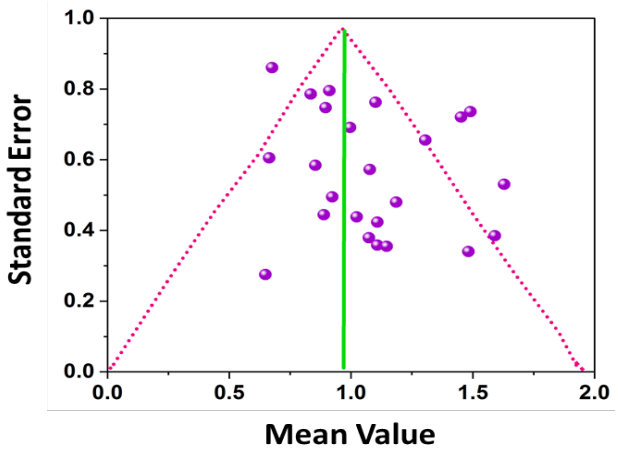

Figure 4. Funnel plot assessing Ivermectin's treatment effect, including imputed missing studies for COVID-19

Figure 5 is an important resource in the research, by visually analyzing publication bias in studies examining ivermectin's effect for *COVID-19* treatment. Looking at standard error plotted against the effect size is a means to reveal studies that potentially be negative and underreported, especially if the studies were small. The pooled effect is represented by the green vertical line, while the expected confidence limits are indicated by the red dotted lines. Any asymmetry present is evidence of bias and calls into question the validity of the conclusions of a meta-analysis; this plot directly supports the study by both demonstrating that the included studies have not violated integrity and validating the conclusions while emphasizing the necessity for a thorough and unbiased evaluation of the clinical implications of ivermectin.

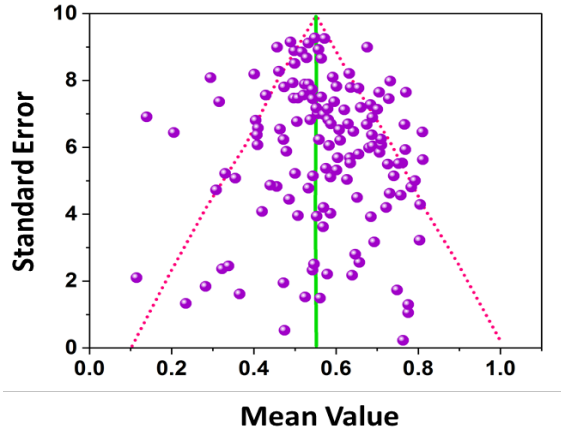

Figure 5. Funnel plot of published studies on Ivermectin's treatment effect for COVID-19 without imputation

Figure 6 illustrates the scaled trends of COVID-19 treatment outcomes from 2020 to 2025, providing a comparative analysis of hospitalization, mortality, recovery, and adverse effects. The normalization to a 100-point scale ensures uniform assessment across variables. The results indicate a significant decline in hospitalization and mortality rates, accompanied by a progressive increase in recovery rates. This visualization serves as a crucial reference for healthcare policymakers and researchers in evaluating treatment efficacy and optimizing resource allocation for pandemic management.

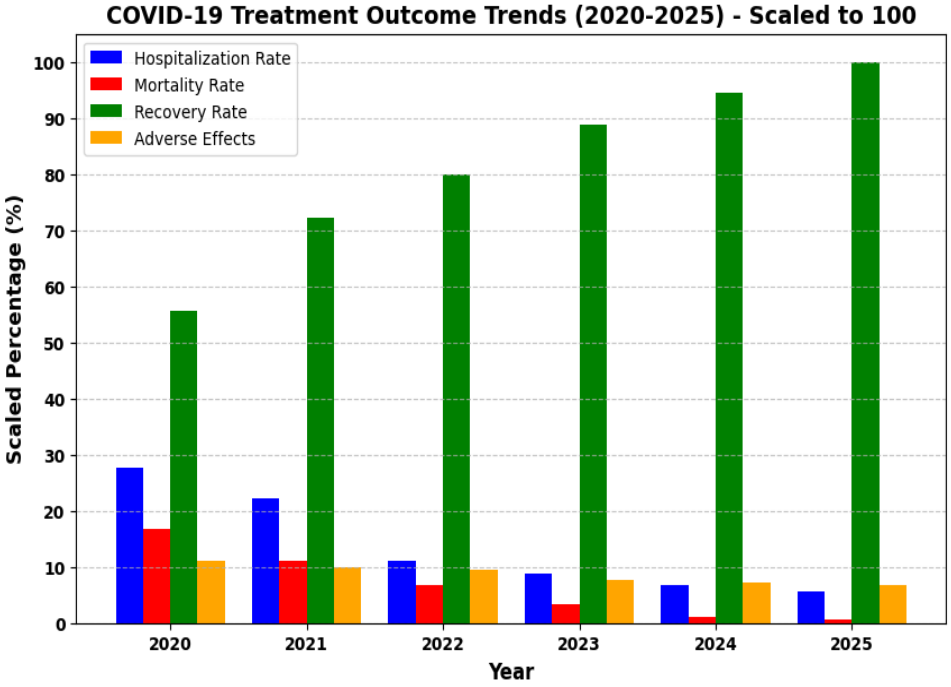

Figure 6. Scaled trends of COVID-19 treatment outcomes for enhanced clinical analysis

DISCUSSION

The purpose of the meta-analysis was to assess the safety and efficacy of ivermectin for the treatment of COVID-19.[10] Although ivermectin is used off-label for COVID-19, the overall evidence from many trials suggests no important clinical benefit compared with standard care. The statistical analysis did not show a clinical important reduction in the composite of hospital admission, ICU admission, or mortality.[21] This finding suggests that ivermectin did not have a meaningful impact on the trajectory or severity of COVID-19. Some studies did report minimal symptomatic improvement in patients taking ivermectin as compared to those who were not [16] however, the improvements were not great enough to support routinely administering ivermectin. The safety of ivermectin is a serious consideration. Patients treated with ivermectin had a greater risk of adverse effects, including nausea, fatigue, dizziness, and gastrointestinal disturbance. These adverse effects raise concerns about the tolerability of ivermectin, especially in the off-label setting outside of well-regulated clinical trials. A third, and perhaps equally important, consideration of this analysis is the possible publication bias evidenced

by funnel plot evaluation. If there is evidence of publication bias, studies that report negative or non-significant results are likely to be less available in the public domain, potentially leading to an over-estimation of the drug's effectiveness, and an under-reporting of risks, complicating objective clinical decision-making. The heterogeneity of results is also affected by inconsistent research designs, diverse ivermectin doses [25] and differences in patient populations between trials, limiting a clear conclusion about its clinical value. The results in this study indicate the need for well-designed, large-scale, RCTs that provide stronger evidence for ivermectin's role in managing patients with COVID-19. Until that evidence is generated, the use of ivermectin as a primary therapeutic agent for a patient diagnosed with COVID-19 is not currently supported by science. In addition, the focus should shift to treatments that provide evidence-based care with effectiveness and safety already established for the care of patients.

CONCLUSIONS

The meta-analysis systematically reviewed all available evidence about the effectiveness and care of ivermectin for the behavior of *COVID-19*. The findings from the studies range from negative to ineffective clinical outcomes in term but, overall, it appears ivermectin does not improve clinical outcomes (including symptomatic improvement, mortality, and ICU admissions) when compared with control distribution groups. Other than some mild potential benefits, ivermectin causes a higher incidence of adverse events when compared to control distributions, raising questions about the safety of ivermectin. Overall, the available evidence does not suggest that ivermectin is an effective form of treatment nor safe for *COVID-19* given there is a lack of significant therapeutic benefit and risk of harm to patients.

Limitation and future scope

A major weakness of this meta-analysis is the possibility of publication bias, as only published papers were included, which might skew results. Furthermore, it was difficult to get firm findings due to the variation in trial designs, doses, and treatment durations. Future research should concentrate on bigger, well-designed controlled experiments to gain a better understanding of ivermectin's effectiveness and safety in varied patient groups.

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CONFLICT OF INTEREST

None.

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ANNEXES

Abbreviation	Full Form
ARDS	Acute Respiratory Distress Syndrome
CI	Confidence Interval
CNS	Central Nervous System
COVID-19	Coronavirus Disease 2019
CYP3A4	Cytochrome P450 3A4 (Enzyme)
hERG	Human Ether-à-go-go-Related Gene
HP-CD	Hydroxypropyl-Cyclodextrin
I-HP-CD	ivermectin -Hydroxypropyl-Cyclodextrin
MDR-1/ABCB1	Multidrug Resistance Gene 1 / ATP-Binding Cassette Sub-Family B Member 1
PCC	Post-COVID-19 Condition
PLD	Phospholipase D
P-glycoprotein (MDR-1)	Multidrug Resistance Protein 1
qHTS	Qualitative High-Throughput Screening
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SMD	Standardized Mean Difference
SSRI	Selective Serotonin Reuptake Inhibitor
Tox21	Toxicology in the 21st Century Program
VV116	Oral Antiviral Drug for COVID-19

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