INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

International Journal of Medical Science and Public Health Research

Journal Website: https://ijmsphr.com/index.php/ijmsphr

Research Article

COMPARATIVE SAFETY EFFICACY OF CONVENTIONAL AND TRADITIONAL MEDICINE FOR COVID-19 TREATMENT: UMBRELLA REVIEW

Submission Date: May 26, 2024, **Accepted Date:** May 31, 2024,
Published Date: June 05, 2024
Crossref Doi: https://doi.org/10.37547/ijmsphr/Volume05Issue06-01

Bukhari
Master of Public Health, Postgraduate, Muhammadiyah University of Aceh, Banda Aceh, Aceh, 23245, Indonesia

Sartika Maulida Putri
Sihat Beurata College of Health Sciences, Banda Aceh, Aceh, 133056, Indonesia

Asnawi Abdullah
Master of Public Health, Postgraduate, Muhammadiyah University of Aceh, Banda Aceh, Aceh, 23245, Indonesia

Hafnidar
Master of Public Health, Postgraduate, Muhammadiyah University of Aceh, Banda Aceh, Aceh, 23245, Indonesia

Fahmi Ichwansyah
Master of Public Health, Postgraduate, Muhammadiyah University of Aceh, Banda Aceh, Aceh, 23245, Indonesia

Hermansyah
Department of Nursing, Health Polytechnic, Ministry of Health, Aceh, 405001, Indonesia

ABSTRACT

Until now, no specific drug to kill the virus that causes COVID-19 has received approval from the Food and Drug Association (FDA). However, the drugs that are often used are off-label antiviral drugs. The research design used is an umbrella review that identifies, assesses and interprets all findings on a systematic review and meta-analysis research topic. This umbrella review research involved 76 studies and 871,985 COVID-19 patients. Statins, colchicine, aspirin and siltuximab are associated with a reduced risk of mortality in COVID-19 patients, but siltuximab has the side effects of cytopenias, infections and hypersensitivity reactions. Remdesivir and umifenovir have the side effect of diarrhea, while ribavirin has the side effect of severe bradycardia in COVID-19 patients. Anakinra, oseltamivir, umifenovir, azithromycin, interferon beta and favipiravir are ineffective and have no significant benefit. Meanwhile, treating

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

COVID-19 with traditional Chinese medicine (TCM) combined with conventional medicine has excellent results, efficacy, and safety effects. Only Jinhua qinggan granule (JHQG) has side effects in the form of mild diarrhea. Further research is needed regarding the concentration of TCM administered to COVID-19 patients, both children and adults.

KEYWORDS

COVID 19, COVID-19 Treatment, 2019-nCov.

INTRODUCTION

Three and a half years after the pandemic outbreak and the World Health Organization (WHO) officially declared that the state of emergency had ended, COVID-19 remains a significant global problem [1]. Even now, a new variant of COVID-19 has emerged, first reported by WHO on 17 February 2023 [2]. Treatment with appropriate drugs is urgently needed to treat COVID-19 patients in the future.

Treatment management and care of COVID-19 patients is currently made on a case-by-case basis, and the decision-making process includes evaluating the severity of clinical presentation, appropriateness of self-isolation, and the likelihood of disease progression requiring hospitalization [3]. Until now, no specific treatment has been used to treat COVID-19 infection directly, but treatment is carried out based on the pathological picture and clinical phase of moderate to severe COVID-19 [4]. Several types of drugs have been used to treat COVID-19 since the early phase of the disease's development, such as corticosteroids, redeliver, hydroxychloroquine, lopinavir-ritonavir, interferon beta, convalescent plasma, azithromycin, colchicine, tocilizumab, favipiravir, umifenovir, ribavirin, dexamethasone, sofosbuvir and tocilizumab [5].

Several clinical trials and observational studies have been conducted to investigate several pharmacological agents and traditional medicines for potentially treating COVID-19 sufferers, but the results obtained have been mixed. Kim et al. said corticosteroids can reduce mortality and increase cure rates without increasing the risk of drug effects on patients compared to standard care [6]. However, other studies show the opposite results, namely that treatment of COVID-19 with corticosteroids does not have any benefits and may be dangerous for COVID-19 patients [3]. Differences in study results also occur in the use of lopinavir for the treatment of COVID-19 patients. Treatment of COVID-19 patients with lopinavir can improve patient recovery and has potential for treating COVID-19 patients [7]. However, another study also came to the opposite conclusion, where the use of lopinavir was not beneficial in treating COVID-19 patients [8].

Several research studies highlight the use of traditional medicines to treat COVID-19 patients, including curcumin, gingerol, and quercetin, which have been proven to function well as pivot molecules and can work against COVID-19 [9]. Lianhua qingwen is currently also used for the prevention and treatment of COVID-19 and has the efficacy of improving clinical symptoms associated with fever, cough, and fatigue and can reduce the severity of COVID-19 and shorten the course of the disease [10]. Interestingly, more than 85% of patients with COVID-19 in China received treatment with TCM approved by the government [11].

Looking at the current phenomenon of care and treatment for COVID-19, where there are still many

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

different study results regarding the drugs used to treat COVID-19 and no instructions for use and recommendations for drugs for the treatment of COVID-19, more studies are needed to study COVID-19 care and treatment. This research aims to provide drug recommendations as a guide for the treatment of COVID-19 based on an evidence base.

METHOD

This research uses the umbrella review method and filters references from 2020 to 2022, as well as systematic review, meta-analysis, full text, and human and English language. Search for keywords by searching for words that are relevant to the words COVID-19 and SARS-COV-2 in the PubMed data base. Next, the article will be coded using the NVIVO application.

The keywords used are COVID 19, COVID-19 Virus Disease, COVID-19 Treatment, COVID-19 Virus Diseases, Disease, COVID-19 Virus, Virus Disease, COVID-19, COVID-19 Virus Infection, COVID 19 Virus Infection, COVID -19 Virus Infections, Infection, COVID-19 Virus, Virus Infection, COVID-19, 2019-nCoV Infection, 2019 nCoV Infection, 2019-nCoV Infections, Infection, 2019-nCoV, Coronavirus Disease-19, Coronavirus Disease 19, 2019 Novel Coronavirus Disease, 2019 Novel Coronavirus Infection, 2019-nCoV Disease, 2019 nCoV Disease, 2019-nCoV Diseases, Disease, 2019-nCoV, COVID-19, Coronavirus Disease 2019, Disease 2019, Coronavirus, SARS Coronavirus 2 Infection, SARS-CoV-2 Infection, infection, SARS-CoV-2, SARS CoV 2 Infection, SARS-CoV-2 Infections, COVID-19 Pandemic, COVID 19 Pandemic and COVID-19 Pandemics. Next, search for keywords that are relevant to SARS-CoV-2, namely Coronavirus Disease 2019 Virus, 2019 Novel, Coronavirus, 2019 Novel Coronaviruses, Coronavirus, 2019 Novel, Novel Coronavirus, Wuhan Seafood Market, Pneumonia Virus, SARS-CoV-2 Virus, SARS CoV 2 Virus, SARS-CoV-2 Viruses, Virus, SARS-CoV-2, 2019-nCoV, COVID-19 Virus, COVID 19 Virus, COVID-19 Viruses, Virus, COVID-19, Coronavirus, Wuhan, SARS Coronavirus 2, Coronavirus 2, SARS and Severe Acute Respiratory Syndrome Coronavirus 2. After all the keywords were used, the article selection process was carried out as explained in Figure 1 so that articles that met the inclusion qualifications in Table 1 were obtained.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

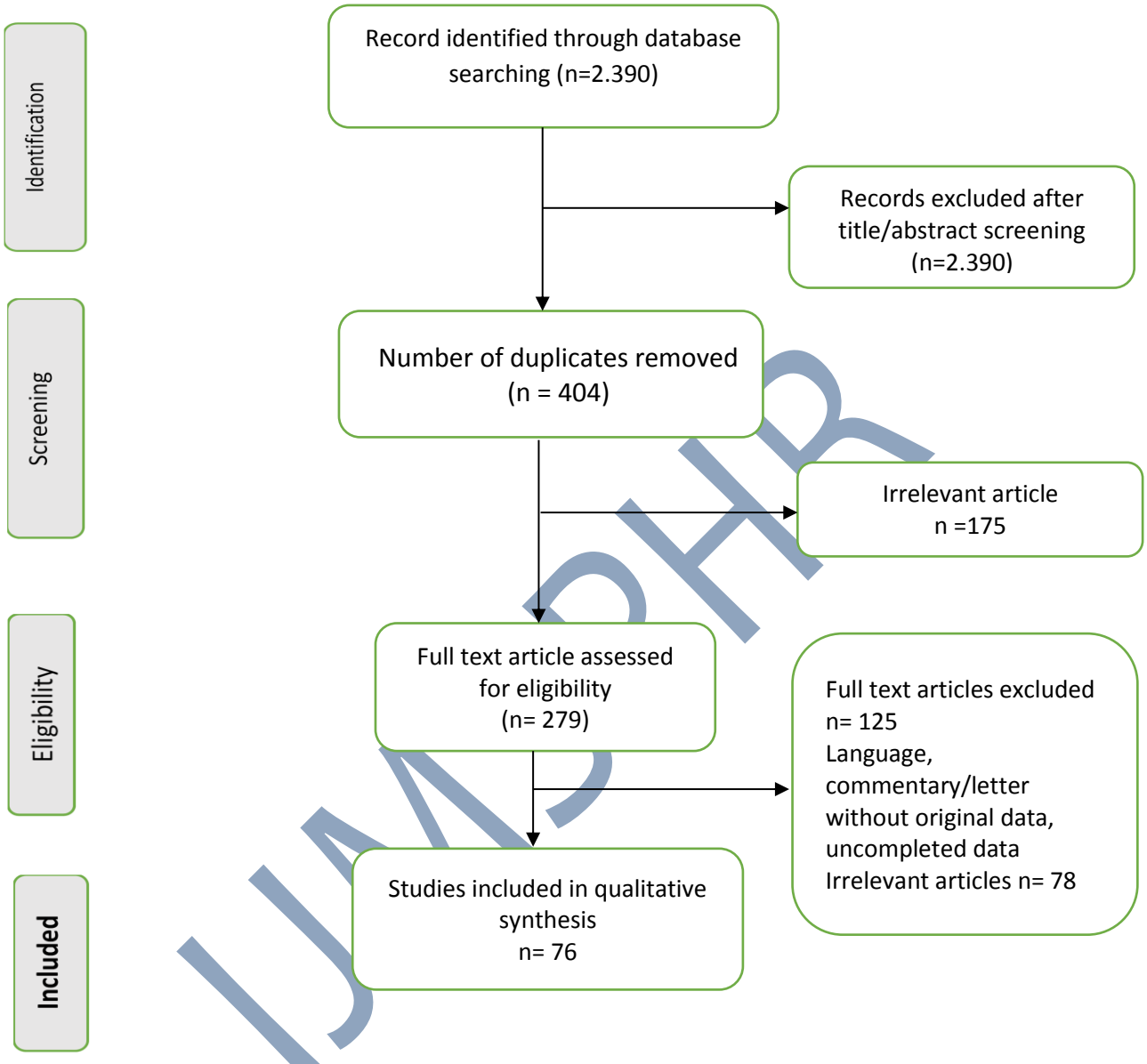

Figure 1. PRISMA diagram of literature search

RESULTS

Table 1. Characteristics of studies included in the inclusion criteria

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

Author, (year)	Study Status	Country	Number of patients	Intervention group	Research design
Alkofide et al. (2021)	Published	Saudi Arabia	5.776	Tocilizumab, corticosteroid	Systematic review Meta analysis
Amani et al. (2021)	Published	Iran	4.652	Arbidol, umifenovir	Systematic review Meta analysis
Avni et al. (2021)	Manuscripts	Israel	6.481	Tocilizumab	Meta analisis
Berardicurti et al. (2020)	Published	Italy	1.520	Tocilizumab	Systematic review Meta analysis
Bhowmick et al. (2021)	Published	Switzerland	8.754	Ivermectin, doxycycline	Scoping review
Bryant et al. (2021)	Published	UK	3.406	Ivermectin	Systematic review Meta analysis
Chaudhry et al. (2021)	Published	Pakistan	6.770	Ivermectin	Systematic review
Chen et al. (2021)	Published	China	11.487	Tocilizumab	Systematic review Meta analysis
Diaz-Arocutipa et al. (2021)	Published	Peru	147. 824	Statins	Meta analysis
Elshafei et al. (2021)	Published	Qatar	5.522	Colchicine	Meta analysis
Golpour et al. (2021)	Published	Iran	NA	Colchicine	Meta analysis
Hariyanto et al. (2021)	Published	Indonesia	5.778	Colchicine	Systematic review Meta analysis
Hassanipour et al. (2021)	Published	Iran	NA	Favipiravir	Systematic review Meta analysis
Heidary & Gharebaghi (2020)	Published	Japan	NA	Ivermectin	Systematic review
Ivan Hariyanto & Kurniawan (2021)	Published	Indonesia	577	Tocilizumab	Systematic review
Joseph et al. (2021)	Published	Saudi arabia	279	Lopinavir/ritonavir	Systematic review
Juul et al. (2021)	Published	Italy	40.249	Remdesivir, lopinavir-ritonavir,	Systematic review Meta Analysis

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

				interferon beta, azithromycin, colchicine	
Kaka et al. (2021)	Published	USA	7.767	Remdesivir	Systematic review Meta analysis
Khan et al. (2021)	Published	London	22.058	Anakinra sarilumab, siltuximab dan tocilizumab	Systematic review Meta analysis
Kinobe & Owens (2021)	Published	Australia	NA	Ivermectin	Systematic review
Kollias et al. (2021)	Published	Greece	72.881	Statin	Systematic review Meta analysis
Kow et al. (2021)	Published	NA	658	Ivermectin	Meta Analysis
Kumar et al. (2021)	Published	Switzerland	NA	Interferon-β	Systematic review Meta analysis
Kyriakopoulos et al. (2021)	Published	Greece	27.004	Tocilizumab	Systematic review Meta analysis
Lan et al. (2020)	Published	China	592	Tocilizumab	Systematic review Meta analysis
Lin et al. (2021)	Published	China	3.267	Tocilizumab	Systematic review Meta analysis
W. Liu et al. (2020)	Published	China	2.060	Ribavirin, chloroquine, hydroxychloroquine, arbidol, favipravir, interferon dan iopinavir/ritonavir	Systematic review Meta analysis
Mahroum et al. (2021)	Published	Israel	15 (531	Tocilizumab	Systematic review Meta analysis
Manabe et al. (2021)	Published	Japan	NA	Favipiravir	Systematic review Meta analysis
Martha et al. (2021)	Published	Indonesia	13.993	Aspirin	Systematic review

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

					Meta analysis
Mikolajewska et al. (2021)	Published	NA	11.525	Colchicine	Systematic review
Musa et al. (2020)	Published	USA	450	Remdesivir	Systematic review
Nakhlband et al. (2021)	Published	Iran	314	Interferon-beta	Systematic review Meta analysis
Nawangsih et al. (2021)	Published	Indonesia	5.530	Colchicine	Systematic review Meta analysis
Nugroho et al. (2021)	Published	Indonesia	6.160	Tocilizumab	Systematic review Meta analysis
Okoli et al. (2021)	Published	Canada	7.540	Remdesivir	Systematic review Meta analysis
Özlüşen et al. (2021)	Published	Germany	1.636	Favipiravir	Systematic review
Pasin et al. (2021)	Published	Italy	184	Anakinra	Meta analysis
Patel et al. (2021)	Published	India	5.040	Lopinavir-ritonavir	Systematic review
Perveen et al. (2020)	Published	Bangladesh	439	Lopinavir-ritonavir, remdesivir, ribavirin dan arbidol	Systematic review
Piscoya et al. (2020)	Published	Peru	4.680	Remdesivir	Systematic review Meta analysis
Popp et al. (2021)	Published	Germany	1.530	Ivermectin	Systematic review
Rakedzon et al. (2021)	Published	Israel	NA	Ivermectin	Systematic review
Rezaei et al. (2021)	Published	Iran	13.189	Tocilizumab	Systematic review Meta analysis
Rezagholizadeh et al. (2021)	Published	Iran	14.888	Remdesivir	Systematic review Meta analysis

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

Rubio-Rivas et al. (2021)	Published	Spain	19.273	Tocilizumab	Systematic review Meta analysis
Sarfraz et al. (2021)	Published	Pakistan	2.120	Tocilizumab	Meta analysis
Selvaraj et al. (2021)	Published	USA	3.358	Tocilizumab	Meta analysis
Shrestha et al. (2020)	Published	Nepal	1.106	Favipiravir	Systematic review Meta analysis
Shrestha et al. (2021)	Published	Nepal	5.694	Remdesivir	Systematic review Meta analysis
Siemieniuk et al. (2020)	Published	Canada	76.767	Azithromycin, lopinavir-ritonavir, interferon beta dan ivermectin	Systematic review Meta analysis
Simmons et al. (2021)	Published	UK	176	Sofosbuvir/daclatasvir	Meta analysis
Singh et al. (2021)	Published	India	7.324	Remdesivir	Systematic review Meta analysis
Snow et al. (2021)	Published	UK	6.493	Tocilizumab	Meta analysis
Solis-García Del Pozo et al. (2020)	Published	Spain	3.788	IL-6	Systematic review
Song et al. (2020)	Published	USA	1.611	Remdesivir, ribavirin, interferon, xuebijing , arbidol, interleukin-6	Systematic review
Srivastava & Kumar (2021)	Published	India	56.696	Aspirin	Meta analysis
Tharmarajah et al. (2021)	Published	UK	4.142	IL-6 inhibition	Meta analysis
Tleyjeh et al. (2021)	Published	Saudi Arabia	5.391	Tocilizumab	Systematic review Meta analysis
Vargas et al. (2020)	Published	Italy	391	Lopinavir/ritonavir	Systematic review

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

Vrachatis et al. (2021)	Published	Italy	881	Colchicine	Meta analysis
Wadaa-Allah et al. (2021)	Published	Egypt	2.079	Favipiravir, lopinavir-ritonavir, arbidol, remedsivir dan tocilizumab	Scoping review
K. S. Wu et al. (2021)	Published	China	63.537	Statins	Systematic review Meta analysis
Xiang et al. (2021)	Published	China	825	IVIG intravenous immunoglobulin)	Meta analysis
Yao et al. (2020)	Published	China	402	Lopinavir-ritonavir, arbidol	Systematic review
Yokoyama et al. (2020)	Published	USA	2.290	Remdesivir	Meta analysis
Zein et al. (2021)	Published	Indonesia	1.788	Ivermectin	Systematic eview Meta analysis
Zhang et al. (2021)	Published	China	102.950	Remdesivir, colchicine, sarilumab, tocilizumab, ivermectin	Meta analysis
Zhang et al. (2020)	Published	Singapore	4.203	Lopinavir-ritonavir	Systematic review Meta analysis
Zhong et al. (2020)	Published	Singapore	4.941	Lopinavir/ritonavir, ribavirin	Systematic review Meta analysis
Du et al. (2021)	Published	China	1.393	Lianhua qingwen capsules, toujie uwen granules, jinyinhua oral liquids, diammonium glycyrrhizinate	Systematic review Meta analysis
A. Y. Fan et al. (2020)	Published	China	732	Jinhua inggan granules,	Systematic review

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

				lianhuaqingwen capsules	Meta analysis
Jin et al. (2020)	Published	China	598	Lianhua qingwen ,qingfei touxie fusheng	Meta analysis
Liang et al. (2021)	Published	China	1.079	LHQW, JHQG, toujie quwen, lianhua qingke	Systematic review Meta nalyasis
Sun et al. (2020)	Published	China	681	Touxie quwen, reyanning mixture, hufengjiedu capsule, Jinhua qinggan granule	Systematic eview Meta analysis
L. P. Zhou et al. (2021)	Published	China	1.285	Jinhua qinggan granule, qingfei touxie fuzheng, toujie quwen granules, lianhua qingke granule, lianhua qingwen capsule	Systematic review Meta analysis

Until now, there are no specific drugs used to kill the virus that causes COVID-19 that have received approval from the FDA, however the drugs that are often used are off-label antiviral drugs Yao et al., 2020). Some of these antiviral drugs have side effects ranging from low, medium to severe. Several studies show different results regarding the efficacy and safety of COVID-19 drugs. From the literature search process to arrive at literature that met the criteria for further review as seen in Figure 1, 15 conventional medicines and 7 traditional medicines were obtained as described in Table 2.

Statin

The discussion of Statins involved three systematic review articles and meta-analysis, and there were more than 220,705 patients, with the lowest age being 44.9 years and the highest being 70.9 years, with the dominant comorbidities being hypertension, diabetes, and cardiovascular disease. Nearly 30% of statin users are patients who have a history of cardiovascular disease [12]. Statins are not associated with mortality in COVID-19 and have even been associated with reduced mortality in COVID-19 patients [12-14]. However, it does not discuss the side effects in COVID-19 patients treated with Statins.

Sofosbuvir/daclatasvir

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

Only one systematic review article met the inclusion criteria regarding Sofosbuvir/daclatasvir. Study Simmons et al. (2021) reviewed three articles and involved 176 COVID-19 patients with a higher 14-day clinical recovery rate in the sofosbuvir/daclatasvir group compared to the control group [RR = 1.34 (95% CI = 1.05-1, 71) P = 0.020]. Cause of death data: 5/92 (5%) in the sofosbuvir/daclatasvir group and 17/84 (20%) in the control group died while enrolled in the trial. The combined risk of all-cause death was significantly lower in the sofosbuvir/daclatasvir group compared with the control group [RR=0.31 (95% CI = 0.12-0.78), P=0.013, I^2=0%. However, the sample size for the analysis was relatively small; one of the trials was not randomized.

Colchicine

This research included Five systematic review studies involving more than 15,000 COVID-19 patients. The average age of patients treated in hospitals is around 55 years to 64 years. Pooled analyses suggest that Colchicine is associated with lower mortality in patients with COVID-19 [16, 18-20, 76]. Colchicine administration has also been associated with improved outcomes in COVID-19 patients [17, 18]. There is no definitive evidence of the effects of Colchine compared to placebo [17].

Aspirin

The discussion regarding the treatment of COVID-19 patients involved two systematic review studies and a meta-analysis involving around 70,689 COVID-19 patients. The results showed that the use of low-dose aspirin was independently associated with reduced mortality (RR = 0.46) with a confidence level of 95% (0.35-0.61), P < 0.001) [21]. Another study showed lower mortality in COVID-19 patients in the aspirin group compared with the non-aspirin group. Odd Ratio (OR) = 0.70 (0.63,-0.77) [22].

Anakinra

One study of the drug Anakinra involving 22,050 patients showed insufficient evidence regarding Anakinra's efficacy in COVID-19; more research is needed to determine the effectiveness of using anakinra in COVID-19 patients [23]. However, another study Pasin et al. (2021) showed that the overall mortality rate in patients treated with anakinra was significantly lower than the mortality in the control group and had a substantially lower risk of needing to use a ventilator than controls. However, the number of COVID-19 patients involved is smaller.

Oseltamivir

A systematic review study examining five RCTs in 439 patients and seventeen cases involving 1,656 patients found that oseltamivir can inhibit the neuraminidase enzyme expressed on the virus's surface. Still, oseltamivir did not show efficacy in COVID-19 antiviral therapy [25].

Umifenovir/Arbidol

The results showed that using Arbidol was ineffective, and no remarkable therapeutic effect was observed [26, 77]. Arbidol is also associated with a high incidence of side effects [26] and possibly causes diarrhea or decreased appetite [28].

Intravenous Immunoglobulin g (IVIg)

Research from Song et al (2020) showed IVIg did not demonstrate any safety or efficacy and is not recommended for the treatment of COVID-19. However, research suggested by Xiang et al. (2021) that IVIg has shown clinical efficacy in critically ill patients

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

with COVID-19. There may be a relationship between the effectiveness of IVIg and the severity of COVID-19 disease, although not significant.

Ribavirin

Compared with control treatment, antiviral intervention with Ribavirin significantly reduced mortality [28, 30]. However, research presented by Perveen et al. (2020) shows the opposite result, namely that there is no evidence of the efficacy of ribavirin therapy as an antiviral. The use of Ribavirin itself has a poor level of safety, causing more bradycardia, anemia, transaminitis, and decreased hemoglobin [28, 30, 77].

Azitromisin

Azithromycin does not have any benefit in the treatment of COVID-19 [31, 32]. The mortality rate in the Hydrochloroquin + Azithromycin group was significantly higher than in the control group, and the duration of hospital stay was shorter in the control group than in the Azithromycin group [32].

Interferon IFN)

The average mortality rate was 6.195% and 18.02% in the IFN-β intervention and control groups [33]. The results of another study from [5] revealed that there was no significant evidence that Interferon β reduced the mortality rate in COVID-19 patients (RR 0.75; 95% CI 0.30 - 1.88; p = 0.54), but virus clearance occurred shorter MD 4, 6 days).

Favipiravir

There is no evidence that Favipiravir can reduce mortality rates or use mechanical ventilation among moderate and severe COVID-19 patients [35]. Overall, Favipiravir may not significantly reduce mortality in the general group of patients with mild to moderate COVID-19 [36]. There was no strong evidence that the use of Favipiravir can cause the side effect of diarrhea [28].

Interleukin-6 tocilizumab, sarilumab, dan siltuximab

Several side effects, such as neutropenia, elevated liver enzymes, and lipid changes, have been reported with tocilizumab, and it is not recommended in patients with severe hepatic or renal failure [31]. Another study revealed that the common side effects of siltuximab were cytopenias, infections, and hypersensitivity reactions; 33% of patients experienced clinical improvement, 43% remained stable, and 24% worsened [77]. However, studies of interleukin-6 may reduce mortality rates [38]. Several other studies have revealed that, in general, interleukin-6 class drugs show a good safety profile and are even associated with reduced mortality rates in COVID-19 patients [38], including tocilizumab [39, 40, 42, 43, 47, 49, 50, 54], and is clinically well tolerated by patients when treated.

Lopinavir/ritonavir

Lopinavir-ritonavir does not appear to have significant benefits and has adverse effects against COVID-19 [31, 77]. Even lopinavir/ritonavir with ribavirin and corticosteroids did not show benefits in reducing mortality rates, and lopinavir/ritonavir was declared ineffective in reducing the SARS-CoV-2 viral load [30]. However, research Fragkou et al. (2020) revealed that Lopinavir-ritonavir significantly reduced adverse effects, including mortality.

Remdesivir

The research results by [66] revealed that Remdesivir can reduce mortality rates, although not significantly. However, the results of this study contradict research

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

conducted by [5, 62, 68] which revealed no reduction in mortality in patients who received remdesivir treatment. Even remdesivir did not show beneficial effects and clinical improvement in COVID-19 patients [5, 64]. However, research results from [67] showed that four randomized controlled trials showed that the rate of clinical improvement was significantly higher in the day five remdesivir group and day ten remdesivir group compared with the standard care group.

DISCUSSION

This systematic review and meta-analysis provide a comprehensive overview of the evidence for treating COVID-19 patients using conventional medicine based on the literature from 2020 to 2022. Statins have been proven to reduce the risk of death by 35% in 220,705 patients, with almost 30% of statin users being patients who have a history of cardiovascular disease. However, there needs to be a detailed discussion regarding the side effects of Satin. Sofosbuvir/daclatasvir also had a lower mortality rate than the control group [RR = 1.34 (95% CI = 1.05-1.71), P = 0.020]. Sofostavir also showed a better clinical recovery rate that was 14 days higher in the sofosbuvir/daclatasvir group compared with the control group [RR = 1.34 (95% CI = 1.05-1.71), P = 0.020]. However, studies on sofosbuvir/daclatasvir had relatively small sample sizes.

Colchicine, aspirin and siltuximab also show a reduced risk of death in CoVID-19 patients. However, siltuximab has the side effects of cytopenia, infections and hypersensitivity reactions. This makes siltuximab have a high level of risk for some patients. Remdesivir and umifenovir also have mild side effects in the form of diarrhoea. In contrast, ribavirin has the side effect of severe bradycardia in COVID-19 patients and does not have significant benefits in reducing mortality rates. Based on these results, this type of drug is not recommended for treating COVID-19 patients. Anakinra, oseltamivir, umifenovir, azithromycin, interferon beta, and favipiravir are ineffective and have no significant benefit in COVID-19 patients.

Meanwhile, the search results for articles regarding traditional medicine in treating COVID-19 are dominated by China, while other countries do not use conventional medicine in treating COVID-19 patients. This is likely because China has a better experience dealing with COVID-19, considering this disease first occurred in China. Traditional medicine used in China, sometimes called TCM, is combined with conventional medicine. Some TCMs used are Lian Hua qing wen capsule (LHQG), diammonium glycyrrhizinate, Jinhua ginggan granule, Dougie queen granule, Lian Hua qingke and remaining. A total of 5 articles reviewing TCM were included in the inclusion criteria and involved 5,036 patients.

TCM is used to treat COVID-19 patients by adding other conventional antiviral drugs. Oral TCM combined with traditional medications can increase the cure rate, shorten the duration of cough, fever and fatigue, and increase the recovery rate [69, 74, 75]. TCM Jinhua qing gan granule, Dougie queen granule, jinyinhua oral liquid, Lian Hua qing wen capsule maxing xuanfei jiu decoction, Lian Hua qingke granule, remaining mixture combined with conventional drugs in the treatment of mild to moderate COVID-19 is better than traditional therapy alone (with a conversion to severe cases [69]. Only JHQG had mild diarrhoea side effects in patients (73).

The research results of Jin et al. (2020) revealed that four types of integrated Chinese and conventional treatment with qingfei tuxie guzheng, Lian Hua qing, and Beijing were significantly superior to symptomatic and supportive treatment alone, except symptomatic and supportive therapy with Lian Hua qing wen. Lianhua qing, when combined with symptomatic and

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

supportive care, is most likely to be the most clinically efficacious intervention.

CONCLUSION

Conventional drugs have varying levels of safety and efficacy in treating COVID-19 patients. However, some conventional drugs have mild to severe side effects. Meanwhile, traditional TCM treatment has excellent results, effectiveness, and safety effects. TCM therapy combined with conventional medications can increase primary clinical and laboratory clinical cure rates and reduce the number of severe cases. The results of this study suggest that health workers always consider the best options for treating COVID-19 patients, such as providing low-risk but highly efficacious drugs.

REFERENCES

1. Biancolella M, Colona VL, Luzzatto L, Watt JL, Mattiuz G, Conticello SG, et al. COVID-19 annual update: a narrative review. Human genomics. 2023;17(1):68.
2. Parums DV. Editorial: A Rapid Global Increase in COVID-19 is Due to the Emergence of the EG.5 (Eris) Subvariant of Omicron SARS-CoV-2. Medical science monitor : international medical journal of experimental and clinical research. 2023;29:e942244.
3. Wadaa-Allah A, Emhamed MS, Sadeq MA, Ben Hadj Dahman N, Ullah I, Farrag NS, et al. Efficacy of the current investigational drugs for the treatment of COVID-19: a scoping review. Ann Med. 2021;53(1):318-34.
4. Stasi C, Fallani S, Voller F, Silvestri C. Treatment for COVID-19: An overview. Eur J Pharmacol. 2020;889:173644.
5. Juul S, Nielsen EE, Feinberg J, Siddiqui F, Jørgensen CK, Barot E, et al. Interventions for treatment of COVID-19: Second edition of a living systematic review with meta-analyses and trial sequential analyses (The LIVING Project). PLoS One. 2021;16(3):e0248132.
6. Kim MS, An MH, Kim WJ, Hwang TH. Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: A systematic review and network meta-analysis. PLoS Med. 2020;17(12):e1003501.
7. Yao TT, Qian JD, Zhu WY, Wang Y, Wang GQ. A systematic review of lopinavir therapy for SARS coronavirus and MERS coronavirus-A possible reference for coronavirus disease-19 treatment option. J Med Virol. 2020;92(6):556-63.
8. Şimşek Yavuz S, Ünal S. Antiviral treatment of COVID-19. Turk J Med Sci. 2020;50(Si-1):611-9.
9. Kumar Verma A, Kumar V, Singh S, Goswami BC, Camps I, Sekar A, et al. Repurposing potential of Ayurvedic medicinal plants derived active principles against SARS-CoV-2 associated target proteins revealed by molecular docking, molecular dynamics and MM-PBSA studies. Biomed Pharmacother. 2021;137:111356.
10. Zhuang J, Dai X, Wu Q, Cai H, Fu X, Zhang W, et al. A meta-analysis for Lianhua Qingwen on the treatment of Coronavirus disease 2019 (COVID-19). Complement Ther Med. 2021;60:102754.
11. Gajewski A, Kośmider A, Nowacka A, Puk O, Wiciński M. Potential of herbal products in prevention and treatment of COVID-19. Literature review. Biomed Pharmacother. 2021;143:112150.
12. Kollias A, Kyriakoulis KG, Kyriakoulis IG, Nitsotolis T, Poulakou G, Stergiou GS, et al. Statin use and mortality in COVID-19 patients: Updated systematic review and meta-analysis. Atherosclerosis. 2021;330:114-21.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

13. Diaz-Arocutipa C, Melgar-Talavera B, Alvarado-Yarasca Á, Saravia-Bartra MM, Cazorla P, Belzusarri I, et al. Statins reduce mortality in patients with COVID-19: an updated meta-analysis of 147 824 patients. Int J Infect Dis. 2021;110:374-81.
14. Wu KS, Lin PC, Chen YS, Pan TC, Tang PL. The use of statins was associated with reduced COVID-19 mortality: a systematic review and meta-analysis. Ann Med. 2021;53(1):874-84.
15. Simmons B, Wentzel H, Mobarak S, Eslami G, Sadeghi A, Ali Asgari A, et al. Sofosbuvir/daclatasvir regimens for the treatment of COVID-19: an individual patient data meta-analysis. J Antimicrob Chemother. 2021;76(2):286-91.
16. Nawangsih EN, Kusmala YY, Rakhmat, II, Handayani DR, Juliastuti H, Wibowo A, et al. Colchicine and mortality in patients with coronavirus disease 2019 (COVID-19) pneumonia: A systematic review, meta-analysis, and meta-regression. Int Immunopharmacol. 2021;96:107723.
17. Mikolajewska A, Fischer AL, Piechotta V, Mueller A, Metzendorf MI, Becker M, et al. Colchicine for the treatment of COVID-19. Cochrane Database Syst Rev. 2021;10(10):Cd015045.
18. Hariyanto TI, Halim DA, Jodhinata C, Yanto TA, Kurniawan A. Colchicine treatment can improve outcomes of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Clin Exp Pharmacol Physiol. 2021;48(6):823-30.
19. Elshafei MN, El-Bardissy A, Khalil A, Danjuma M, Mubasher M, Abubeker IY, et al. Colchicine use might be associated with lower mortality in COVID-19 patients: A meta-analysis. Eur J Clin Invest. 2021;51(9):e13645.
20. Golpour M, Mousavi T, Alimohammadi M, Mosayebian A, Shiran M, Alizadeh Navaei R, et al. The effectiveness of Colchicine as an anti-inflammatory drug in the treatment of coronavirus disease 2019: Meta-analysis. Int J Immunopathol Pharmacol. 2021;35:20587384211031763.
21. Martha JW, Pranata R, Lim MA, Wibowo A, Akbar MR. Active prescription of low-dose aspirin during or prior to hospitalization and mortality in COVID-19: A systematic review and meta-analysis of adjusted effect estimates. Int J Infect Dis. 2021;108:6-12.
22. Srivastava R, Kumar A. Use of aspirin in reduction of mortality of COVID-19 patients: A meta-analysis. Int J Clin Pract. 2021;75(11):e14515.
23. Khan FA, Stewart I, Fabbri L, Moss S, Robinson K, Smyth AR, et al. Systematic review and meta-analysis of anakinra, sarilumab, siltuximab and tocilizumab for COVID-19. Thorax. 2021;76(9):907-19.
24. Pasin L, Cavalli G, Navalesi P, Sella N, Landoni G, Yavorovskiy AG, et al. Anakinra for patients with COVID-19: a meta-analysis of non-randomized cohort studies. Eur J Intern Med. 2021;86:34-40.
25. Perveen RA, Nasir M, Talha KA, Selina F, Islam MA. Systematic review on current antiviral therapy in COVID-19 pandemic. Med J Malaysia. 2020;75(6):710-6.
26. Amani B, Amani B, Zareei S, Zareei M. Efficacy and safety of arbidol (umifenovir) in patients with COVID-19: A systematic review and meta-analysis. Immun Inflamm Dis. 2021;9(4):1197-208.
27. Song Y, Zhang M, Yin L, Wang K, Zhou Y, Zhou M, et al. COVID-19 treatment: close to a cure? A rapid review of pharmacotherapies for the

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

novel coronavirus (SARS-CoV-2). Int J Antimicrob Agents. 2020;56(2):106080.

28. Liu W, Zhou P, Chen K, Ye Z, Liu F, Li X, et al. Efficacy and safety of antiviral treatment for COVID-19 from evidence in studies of SARS-CoV-2 and other acute viral infections: a systematic review and meta-analysis. Cmaj. 2020;192(27):E734-e44.

29. Xiang HR, Cheng X, Li Y, Luo WW, Zhang QZ, Peng WX. Efficacy of IVIG (intravenous immunoglobulin) for corona virus disease 2019 (COVID-19): A meta-analysis. Int Immunopharmacol. 2021;96:107732.

30. Zhong H, Wang Y, Zhang ZL, Liu YX, Le KJ, Cui M, et al. Efficacy and safety of current therapeutic options for COVID-19 - lessons to be learnt from SARS and MERS epidemic: A systematic review and meta-analysis. Pharmacol Res. 2020;157:104872.

31. Siemieniuk RA, Bartoszko JJ, Ge L, Zeraatkar D, Izcovich A, Kum E, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. Bmj. 2020;370:m2980.

32. Ghazy RM, Almaghraby A, Shaaban R, Kamal A, Beshir H, Moursi A, et al. A systematic review and meta-analysis on chloroquine and hydroxychloroquine as monotherapy or combined with azithromycin in COVID-19 treatment. Sci Rep. 2020;10(1):22139.

33. Nakhlband A, Fakhari A, Azizi H. Interferon-beta offers promising avenues to COVID-19 treatment: a systematic review and meta-analysis of clinical trial studies. Naunyn Schmiedebergs Arch Pharmacol. 2021;394(5):829-38.

34. Manabe T, Kambayashi D, Akatsu H, Kudo K. Favipiravir for the treatment of patients with COVID-19: a systematic review and meta-analysis. BMC Infect Dis. 2021;21(1):489.

35. Özlüşen B, Kozan Ş, Akcan RE, Kalender M, Yaprak D, Peltek İ B, et al. Effectiveness of favipiravir in COVID-19: a live systematic review. Eur J Clin Microbiol Infect Dis. 2021;40(12):2575-83.

36. Hassanipour S, Arab-Zozani M, Amani B, Heidarzad F, Fathalipour M, Martinez-de-Hoyo R. The efficacy and safety of Favipiravir in treatment of COVID-19: a systematic review and meta-analysis of clinical trials. Sci Rep. 2021;11(1):11022.

37. Wang D, Li Z, Liu Y. An overview of the safety, clinical application and antiviral research of the COVID-19 therapeutics. J Infect Public Health. 2020;13(10):1405-14.

38. Tharmarajah E, Buazon A, Patel V, Hannah JR, Adas M, Allen VB, et al. IL-6 inhibition in the treatment of COVID-19: A meta-analysis and meta-regression. J Infect. 2021;82(5):178-85.

39. Alkofide H, Almohaizeie A, Almuhaini S, Alotaibi B, Alkharfy KM. Tocilizumab and Systemic Corticosteroids in the Management of Patients with COVID-19: A Systematic Review and Meta-Analysis. Int J Infect Dis. 2021;110:320-9.

40. Avni T, Leibovici L, Cohen I, Atamna A, Guz D, Paul M, et al. Tocilizumab in the treatment of COVID-19-a meta-analysis. Qjm. 2021;114(8):577-86.

41. Berardicurti O, Conforti A, Ruscitti P, Cipriani P, Giacomelli R. The wide spectrum of Kawasaki-like disease associated with SARS-CoV-2 infection. Expert Rev Clin Immunol. 2020;16(12):1205-15.

42. Chen CX, Hu F, Wei J, Yuan LT, Wen TM, Gale RP, et al. Systematic review and meta-analysis of tocilizumab in persons with coronavirus disease-2019 (COVID-19). Leukemia. 2021;35(6):1661-70.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

43. Kyriakopoulos C, Ntritsos G, Gogali A, Milionis H, Evangelou E, Kostikas K. Tocilizumab administration for the treatment of hospitalized patients with COVID-19: A systematic review and meta-analysis. Respirology. 2021;26(11):1027-40.
44. Lan SH, Lai CC, Huang HT, Chang SP, Lu LC, Hsueh PR. Tocilizumab for severe COVID-19: a systematic review and meta-analysis. Int J Antimicrob Agents. 2020;56(3):106103.
45. Lin WT, Hung SH, Lai CC, Wang CY, Chen CH. The effect of tocilizumab on COVID-19 patient mortality: A systematic review and meta-analysis of randomized controlled trials. Int Immunopharmacol. 2021;96:107602.
46. Mahroum N, Watad A, Bridgewood C, Mansour M, Nasr A, Hussein A, et al. Systematic Review and Meta-Analysis of Tocilizumab Therapy versus Standard of Care in over 15,000 COVID-19 Pneumonia Patients during the First Eight Months of the Pandemic. Int J Environ Res Public Health. 2021;18(17).
47. Nugroho CW, Suryantoro SD, Yuliasih Y, Rosyid AN, Asmarawati TP, Andrianto L, et al. Optimal use of tocilizumab for severe and critical COVID-19: a systematic review and meta-analysis. F1000Res. 2021;10:73.
48. Rezaei S, Fatemi B, Karimi Majd Z, Minaei H, Peikanpour M, Anjidani N, et al. Efficacy and safety of Tocilizumab in severe and critical COVID-19: A Systematic Review and Meta-Analysis. Expert Rev Clin Immunol. 2021;17(5):499-511.
49. Rubio-Rivas M, Forero CG, Mora-Luján JM, Montero A, Formiga F, Homs NA, et al. Beneficial and harmful outcomes of tocilizumab in severe COVID-19: A systematic review and meta-analysis. Pharmacotherapy. 2021;41(11):884-906.
50. Sarfraz A, Sarfraz Z, Sarfraz M, Aftab H, Pervaiz Z. Tocilizumab and COVID-19: a meta-analysis of 2120 patients with severe disease and implications for clinical trial methodologies. Turk J Med Sci. 2021;51(3):890-7.
51. Selvaraj V, Khan MS, Bavishi C, Dapaah-Afriyie K, Finn A, Lal A, et al. Tocilizumab in Hospitalized Patients with COVID-19: A Meta Analysis of Randomized Controlled Trials. Lung. 2021;199(3):239-48.
52. Snow TAC, Saleem N, Ambler G, Nastouli E, Singer M, Arulkumaran N. Tocilizumab in COVID-19: a meta-analysis, trial sequential analysis, and meta-regression of randomized-controlled trials. Intensive Care Med. 2021;47(6):641-52.
53. Solis-García Del Pozo J, Galindo MF, Nava E, Jordán J. A systematic review on the efficacy and safety of IL-6 modulatory drugs in the treatment of COVID-19 patients. Eur Rev Med Pharmacol Sci. 2020;24(13):7475-84.
54. Berardicurti O, Ruscitti P, Ursini F, D'Andrea S, Ciaffi J, Meliconi R, et al. Mortality in tocilizumab-treated patients with COVID-19: a systematic review and meta-analysis. Clin Exp Rheumatol. 2020;38(6):1247-54.
55. Chen MR, Kuo HC, Lee YJ, Chi H, Li SC, Lee HC, et al. Phenotype, Susceptibility, Autoimmunity, and Immunotherapy Between Kawasaki Disease and Coronavirus Disease-19 Associated Multisystem Inflammatory Syndrome in Children. Front Immunol. 2021;12:632890.
56. Joseph BA, Dibas M, Evanson KW, Paranjape G, Vegivinti CTR, Selvan PT, et al. Efficacy and safety of lopinavir/ritonavir in the treatment of COVID-19: A systematic review. Expert Rev Anti Infect Ther. 2021;19(6):679-87.
57. Fragkou PC, Belhadi D, Peiffer-Smadja N, Moschopoulos CD, Lescure FX, Janocha H, et al.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

Review of trials currently testing treatment and prevention of COVID-19. Clin Microbiol Infect. 2020;26(8):988-98.

58. Axfors C, Schmitt AM, Janiaud P, Van't Hooft J, Abd-Elsalam S, Abdo EF, et al. Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19 from an international collaborative meta-analysis of randomized trials. Nat Commun. 2021;12(1):2349.

59. Wang Y, Lu C, Li H, Qi W, Ruan L, Bian Y, et al. Efficacy and safety assessment of severe COVID-19 patients with Chinese medicine: A retrospective case series study at early stage of the COVID-19 epidemic in Wuhan, China. J Ethnopharmacol. 2021;277:113888.

60. Vargas M, Servillo G, Einav S. Lopinavir/ritonavir for the treatment of SARS, MERS and COVID-19: a systematic review. Eur Rev Med Pharmacol Sci. 2020;24(16):8592-605.

61. Song G, Qiao W, Wang X, Yu X. Association of Lung Ultrasound Score with Mortality and Severity of COVID-19: A Meta-Analysis and Trial Sequential Analysis. Int J Infect Dis. 2021;108:603-9.

62. Kaka AS, MacDonald R, Greer N, Vela K, Duan-Porter W, Obley A, et al. Major Update: Remdesivir for Adults With COVID-19 : A Living Systematic Review and Meta-analysis for the American College of Physicians Practice Points. Ann Intern Med. 2021;174(5):663-72.

63. Musa A, Pendi K, Hashemi A, Warbasse E, Kouyoumjian S, Yousif J, et al. Remdesivir for the Treatment of COVID-19: A Systematic Review of the Literature. West J Emerg Med. 2020;21(4):737-41.

64. Okoli GN, Rabbani R, Copstein L, Al-Juboori A, Askin N, Abou-Setta AM. Remdesivir for coronavirus disease 2019 (COVID-19): a systematic review with meta-analysis and trial sequential analysis of randomized controlled trials. Infect Dis (Lond). 2021;53(9):691-9.

65. Rezagholizadeh A, Khiali S, Sarbakhsh P, Entezari-Maleki T. Remdesivir for treatment of COVID-19; an updated systematic review and meta-analysis. Eur J Pharmacol. 2021;897:173926.

66. Shrestha DB, Budhathoki P, Syed NI, Rawal E, Raut S, Khadka S. Remdesivir: A potential game-changer or just a myth? A systematic review and meta-analysis. Life Sci. 2021;264:118663.

67. Yokoyama Y, Briasoulis A, Takagi H, Kuno T. Effect of remdesivir on patients with COVID-19: A network meta-analysis of randomized control trials. Virus Res. 2020;288:198137.

68. Singh S, Khera D, Chugh A, Khera PS, Chugh VK. Efficacy and safety of remdesivir in COVID-19 caused by SARS-CoV-2: a systematic review and meta-analysis. BMJ Open. 2021;11(6):e048416.

69. Du X, Shi L, Cao W, Zuo B, Zhou A. Add-on effect of Chinese herbal medicine in the treatment of mild to moderate COVID-19: A systematic review and meta-analysis. PLoS One. 2021;16(8):e0256429.

70. Jin L, Xu Y, Yuan H. Effects of four types of integrated Chinese and Western medicines for the treatment of COVID-19 in China: a network meta-analysis. Rev Assoc Med Bras (1992). 2020;66(6):771-7.

71. Zhou H, Chen D, Zhang Y, Zhu Q, Yang Y, Liu Y, et al. Efficacy and safety of Xiyanping for COVID-2019: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2020;99(46):e22962.

72. Wang Y, Han L, Zhang W, Sun J. The curative effect of Reduning injection combined with Xuanfeibaidu formula on COVID-19: A protocol

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2767-3774)
VOLUME 05 ISSUE 06 Pages: 8-26
OCLC –1242424495

for systematic review and meta-analysis. Medicine (Baltimore). 2020;99(46):e22830.

73. Liang SB, Fang M, Liang CH, Lan HD, Shen C, Yan LJ, et al. Therapeutic effects and safety of oral Chinese patent medicine for COVID-19: A rapid systematic review and meta-analysis of randomized controlled trials. Complement Ther Med. 2021;60:102744.

74. Sun CY, Sun YL, Li XM. The role of Chinese medicine in COVID-19 pneumonia: A systematic review and meta-analysis. Am J Emerg Med. 2020;38(10):2153-9.

75. Zhou LP, Wang J, Xie RH, Pakhale S, Krewski D, Cameron DW, et al. The Effects of Traditional Chinese Medicine as an Auxiliary Treatment for COVID-19: A Systematic Review and Meta-Analysis. J Altern Complement Med. 2021;27(3):225-37.

76. Vrachatis DA, Giannopoulos GV, Giotaki SG, Raisakis K, Kossyvakis C, Iliodromitis KE, et al. Impact of colchicine on mortality in patients with COVID-19: A meta-analysis. Hellenic J Cardiol. 2021;62(5):374-7.

77. Song LG, Xie QX, Lao HL, Lv ZY. Human coronaviruses and therapeutic drug discovery. Infect Dis Poverty. 2021;10(1):28.

78.