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Review Article

Integration of Complementary and Alternative Medicines in Health care system to combat COVID 19- A Validation

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Abstract

Human mankind has always been under the wrath of various epidemics viz. Spanish Flu, Asian Flu, Hong Kong Flu, influenza A-H1N1 virus, SARS in 2003, etc. The on-going COVID 19 pandemic has posed as a serious concern to humans with no proper treatment and no specific drugs against this virus. There have been various challenges to the current health care delivery system. There is dearth of reported RCTs evaluating effects of antivirals. Corticosteroid treatment has reported to have delayed coronavirus RNA clearance with its widespread use leading to development/exacerbation of fungal diseases like Mucormycosis. Various vaccines designed have many questions about their efficacy that may rise with time, as SARS-CoV-2 has numerous variants, and it can mutate over time. With limited success in developing antivirals, Complementary and Alternative medicines like Traditional Chinese medicines, Ayurvedic and homoeopathic medicines have been gaining momentums in recent years displaying promising results. Methodical researches are warranted to further evaluate the efficacy of Complementary and alternative medicines. For curtailing the devastating effects of COVID 19 requires reviewing the current health policies by integrating complementary medicine with conventional system. To channelize all the available therapeutic options to win the battle against COVID-19 is the need of hour.

Keywords: Ayurved, Complementary and alternative medicines, COVID-19, Homoeopathy SARS-CoV-2, Traditional Chinese medicines.

INTRODUCTION

With the discovery of tobacco mosaic virus in 1892 and foot-and-mouth disease virus in 1898, the first to be discovered in humans was the yellow fever virus in 1901.¹ There are 219 virus species that are known to be able to infect humans.² Human mankind has always been under the wrath of epidemics. Three influenza pandemics occurred during the 20th century, the most severe of which was the "Spanish Flu" in 1918–1919 caused by an A(H1N1) virus) with estimated 20–50 million deaths. In 1957–1958 the "Asian Flu" caused by an A (H2N2) virus and in 1968 the "Hong Kong Flu" caused by H3N2 virus with estimated 1–4 million deaths each. The first influenza pandemic of the 21st century in 2009–2010 was caused by an influenza A (H1N1) virus.³

In 2003, an outbreak of new infectious disease severe acute respiratory syndrome (SARS) caused tremendous social, political and economic disruptions in many countries across the world. From China the SARS virus spread to 30 countries. Due to the many questions remaining unanswered about SARS, World Health Organization (WHO) had warned that, "Continued global vigilance for SARS is crucial for the foreseeable future. The world is not yet SARS-free. SARS will continue to menace the global public health system. It is likely the virus still circulates in an animal reservoir and may

cross into humans again when conditions are favourable". It was believed that SARS was a warning.^{4,5}

Looking into the recent outbreaks of H1N1, hCoV, Hendra virus, Nipah virus, and MERS-CoV the Asia-Pacific region seems to be the global hot-spot for the emergence of novel RNA viruses. With human demographic history an estimation of 1 such event per 100 years is broadly consistent⁶

SARS-CoV-2 appeared in 2019 and rapidly spread to over 200 countries. With its rapid global spread re-emergence of the virus after alterations in its genome for stable adaptation is a serious concern to human health. It has a zoonotic origin from bats and animals to humans. With the sequencing and phylogenetic analysis done, it is found that this virus is novel with no cure for its infection. Its genome has similarities with those of SARS-CoV and MERS-CoV but due to mutations in the genome, it became a novel virus. It causes infections with mild symptoms viz. fever, flu, and cough to severe symptoms with clinical outcomes ARDS, septic shock, respiratory failure, and multi-organ dysfunction. With no specific drugs against this virus, and few vaccines been approved, preventive strategies still remain the mainstay. Diligent efforts are being done for identifying an effective treatment against the virus through various therapeutic targets which are involved in the host-virus interaction i.e., proteins, enzymes, pathways, and receptors. Various vaccines designed by using different techniques have been approved.

The SARS-CoV-2 has several variants, and has potential to mutate in population over time. Therefore, many questions about the efficacy of vaccines may rise with time. Vaccines are approved for emergency use; however, they have not been fully evaluated for efficacy against SARS-CoV-2 variants that recently emerged in the UK, South Africa and India.⁷

CHALLENGES TO EXISTING HEALTH CARE SYSTEM

COVID-19 has been an ongoing pandemic with no curative treatment. Treatment of hospitalized patients with symptomatic COVID comprises of supportive care, including oxygenation, mechanical ventilation, hemodynamic support with management of co-morbidities and complications. Various therapies have been proposed for the treatment and are currently being used but are further being tested for their safety and effectiveness. With no specific drugs available for COVID-19 to date different combinations of medicines and therapies are being used to treat patients. Antiviral and anti-inflammatory treatments have been utilized.⁷

Though evidence of favipiravir in COVID-19 shows its usefulness in the management of mild to moderate COVID-19; however whether its effect translates to clinical benefits like shortening the disease course, early hospital discharge, and reducing the oxygen requirement prerequisites large randomized controlled trials.⁸

Despite showing strong antiviral effects in preclinical models of infection with coronaviruses intravenous remdesivir was not found to significantly improve the time to clinical improvement, mortality, or time to virus clearance compared with placebo. Remdesivir did not result in significant reductions in SARS-CoV-2 RNA loads or detectability in upper respiratory tract or sputum specimens. Rather a higher proportion of remdesivir recipients than placebo recipients had to prematurely stop dosing due of adverse events including gastrointestinal symptoms (anorexia, nausea, and vomiting), aminotransferase or bilirubin increases, and worsened cardiopulmonary status. Intravenous remdesivir did not produce substantial clinical and antiviral effects in critical patients with COVID-19.⁹

RCTs evaluating effects of remdesivir in hospitalized COVID-19 patients are deficit. Important questions remains unclear regarding the efficacy of remdesivir viz. the optimal duration of therapy, effect on discrete clinical outcomes, the relative effect of the drug if given in the presence of dexamethasone or other corticosteroids. Until stronger evidence emerges, it cannot be concluded that remdesivir is efficacious for treating COVID-19.^{10, 11}

Corticosteroid therapy was commonly used among critically ill patients with Middle East Respiratory Syndrome (MERS), but its impact on outcomes was uncertain. Corticosteroid therapy in patients with MERS was not associated with a difference in mortality but was associated with delayed MERS coronavirus RNA clearance.¹²

The outcome of corticosteroid on the viral load of Severe Acute Respiratory Syndrome (SARS) patients is unidentified. A higher plasma viral load is associated with early corticosteroid treatment.¹³

COVID-19 due to its immune dysregulation is associated with a significant incidence of secondary infections, both bacterial and fungal probably. Additionally, the widespread use of steroids/monoclonal antibodies/broad-spectrum antibiotics against COVID-19 may have lead to the development/exacerbation of fungal diseases.¹⁴ Uncontrolled diabetes and over-zealous use of steroids are aggravating the illness with

new manifestations appearing over time like the mucormycosis.¹⁵

It is not clear whether a vaccine will confer long-term immunity like measles or short-term immunity as with flu. Unless a vaccine is given to all eight billion inhabitants of the world who are not currently sick or recovered, COVID-19 is likely to become endemic¹⁶.

The coronavirus data from Seychelles reported more than a third of people who tested positive for COVID-19 had been fully vaccinated. Some 37% of those testing positive had received both doses of a vaccine. The WHO said vaccination alone would not stop transmission entirely, and preventive health measures such as social distancing, mask-wearing and hand washing has to continue.¹⁷

The coronavirus, like most viruses, will live on. Estimates about the culmination of COVID-19 pandemic are speculative, but it will most likely involve a blend of factors that mediated in the past pandemics¹⁶.

In controlling 2003 SARS pandemic twenty-first century science played a relatively small role; nineteenth-century techniques continued to prove their value.⁴ There are good reasons for us to learn from ancient wisdom and accumulated clinical experience, in combination with cutting edge science and technologies, to fight with the devastating COVID-19 pandemic now and emerging new viruses in the future.

COMPLEMENTARY MEDICINE AN OPTION TO COUNTER COVID 19

The integration of traditional and modern medicine may offer valuable experience and can contribute for an all-around progress in human medicine is as evident from the ongoing global fight against COVID-19.¹⁸ In the treatment of viral infections natural products and their derivatives have shown potential activities.^{19, 20}

In the inhibition and treatment of respiratory diseases Traditional Chinese Medicine (TCM) has suggested clinical experiences, effective and applicable herbal formulas²¹ When COVID-19 wrecked in Wuhan, China patients admitted to the TCM Hospital were immediately treated with TCM and reported with >90% efficacy. TCM was based on the TCM theory of restoring the human immune system, thus conquering the viral infection indirectly.²² A range of Chinese herbal medicines have been documented to have very promising anti-SARS-CoV-2 agents having potential activity against SARS-CoV-2 and have attracted significant attention due to their activities both in vitro and in clinical practice.²³ Some studies showed that Chinese herbal formula may be associated with blocking of the viral proliferation²⁴

During the Severe Acute Respiratory Syndrome (SARS) epidemic TCM was effective. It was reported that about 85% of COVID-19 patients received combined treatment with TCM and regular medication. Positive outcomes of TCM treatment have been reported. In research laboratory settings antiviral and immune modulation properties have been shown by herbs and their phytoactive components with serious consideration been given to further rigorous scientific studies even outside of China. The potential contribution of TCM to health and well-being has been highlighted in the WHO global report on Traditional and Complementary Medicine.^{25, 26, 27, 28, 29} Chinese medicinal herbs could be an alternative strategy for the prevention of COVID-19 in high-risk populations.³⁰ TCM is mentioned to be the best choice for the treatment and prevention and is expected to be promoted.³¹

Presently, there is good evidence that it has role in affecting the transcription, replication, binding of SARS-CoV-2 and tempering the cytokine storm. TCM can effectively alleviate the symptoms of suspected and confirmed COVID-19 by delaying the progression of disease thereby reducing the mortality.³² Though combination of western medicine and TCM in treatment were documented of great significance for the prevention and treatment of COVID-19 further relevant laboratory research and clinical evaluation is needed to collect scientific evidences on its efficacy.³³

For the treatment of several diseases Indian medicinal plants have been a promising field³⁴. Ayurveda and Siddha practices originated in India and are still commonly used among the Indian population. In addition, identification of phyto-components of medicinal plants may be helpful. Therefore, Indian medicinal plants can be deliberated as an added option for their role to combat viral infections³⁵.

There are reports of beneficial outcomes of Ayurvedic interventions in hypoxia that seems to have the potential to supplement standard of care for COVID-19. Ayurvedic intervention in early stages of decreasing peripheral oxygen saturation could possibly prevent the need for oxygen supplementation and hospitalization. To explore the option of incorporating the Ayurvedic treatment with standard care rigorous clinical studies need to be undertaken³⁶.

The role of Homeopathic medicines have been reportedly documented for the prevention of Cholera, Spanish Influenza, Yellow fever, Scarlet fever, Diphtheria, Typhoid, etc.³⁷ The homoeopathic intervention has played a considerable role in managing Spanish Flu 1918 pandemic not only by treating but also by reducing the mortality³⁸. Usefulness of homoeopathic medicine Bryonia alba 30C as Genus Epidemicus for the prevention of chikungunya is also documented³⁹. Studies have also shown that homeopathy may be an effective adjunct in Dengue outbreak prevention.^{40, 41} In the 2009 pandemic of A/H1N1 influenza, contribution with regard to influenza-like illness has also been done.^{42, 43}

Catalonia, Spain reported positive outcomes of homoeopathic treatment in mild and moderate cases of COVID 19⁴⁴. Various studies are being undertaken in different settings in India, a few aimed at prophylaxis and others aimed at treatment the outcomes of which might provide evidence for clinically repurposing homeopathy's medicines in COVID-19 as an adjuvant or stand-alone⁴⁵.

Homoeopathic medicines cause immune modulating changes through various mechanisms and thus are suggestive of being useful in boosting the immunological responses in various conditions⁴⁶ so possibly will prove as an excellent alternative in COVID 19 treatment.

THE RATIONALE FOR INTEGRATION OF COMPLEMENTARY MEDICINE

Although biomedical knowledge has made a noteworthy progress, there has been recurrent emergence and re-emergence of deadly viral infections widely affecting human health. Though with a large mammalian viruses being identified, there are large numbers of evolving viruses in the offing to adapt and infect⁴⁷. It seems predictable that new viruses will continue to emerge. The emergence of new viruses is a long-standing and continuing biological progression. It is unclear whether this process will eventually slow down or stop or whether it will continue indefinitely if a significant proportion of newly discovered virus species are newly evolved. If anthropogenic drivers of

this process are important then it is possible that we are in the midst of a period of particularly rapid virus emergence⁴⁸.

The unavoidable conclusion is that we must anticipate the emergence and/or discovery of more new human viruses in the coming years and decades.⁴⁸ By no means all of these will pose a serious risk to public health but, if the recent past is a reliable guide to the immediate future, it is very likely that some will.⁴⁸

With the unpredictable nature of novel infections, there is a further need for devoted research to understand the new viral pathogens and human susceptibilities and to develop counter-measures.⁴⁷

With limited success in developing broad spectrum antivirals especially for RNA viruses, herbal medicines used in traditional Chinese or Indian system of medicine are generally considered "safe" due to their widespread use over centuries. Though assessing efficacy of traditional herbal remedies are often difficult due to inadequate, inconsistent methods being used across studies and lack of similar rigor like other medical research in researches involving herbal remedies. Randomized clinical trials involving herbal remedies conducted with sound and consistent methodology are the necessity of this hour.⁴⁹

With no robust evidence for effective prevention and specific therapy at the global level to combat this COVID-19 pandemic, Complementary and Integrative Medicine (CIM) holds a substantial potential for building resilience using herbs and so it should be subjected to further scientific attention and clinical research. From substantial preclinical and limited clinical research it's known that many botanicals have properties that protect against respiratory viruses.

CIM offers a variety of easily feasible, accessible, evidence-based preventive and therapeutic options for respiratory infections and for strengthening physical and mental resilience, likely to also help in prevention and treatment of COVID-19. Although the literature on CIM topics is gradually increasing, high-quality evidence is still lacking. Particularly, further clinical research is needed, including methodologically high-quality studies. All this would require a national and national initiative to facilitate the necessary substantial research to define possible contributions of CIM in the COVID-19 pandemic and beyond.⁵⁰

In addition, preclinical and clinical trial evaluations of CIM for COVID-19 have not specifically been conducted, so further investigations related to this are warranted.⁵¹ Although, traditional Chinese herbal medicine in used for COVID-19 pneumonia, its efficacy remains uncertain.⁵²

In a bibliometric analysis of global research trends at the intersection of COVID-19 and Traditional, integrative, complementary and alternative medicines (TICAMs) findings include the fact that a wide-range of TICAMs have been mentioned across articles; a total of 327 TICAMs were mentioned across the 296 eligible articles with the vast majority of them including traditional Chinese medicine. Eligible articles were published by authors with affiliations in 56 countries, the most common of which included China, the United States, India and Italy.⁵³

Chinese, Indian and Iranian herbal medicine with 1000 years' experience in the prevention of pandemic and endemic infectious diseases are providing as an alternative contender for controlling COVID-19 infection. This is the biggest opportunity to test complementary medicines. Hopefully, positive results from clinical trial experiments explicate the positive effects of Chinese, Indian and Iranian herbal medicine alone and as adjuvant to recovery of SARS-

CoV-2 with further studies needed to discover the novel anti-COVID-19 substances.⁵⁴

India has a pluralistic system for health care delivery wherein along with the conventional medicine coexists the traditional systems of medicine such as Ayurveda, yoga and naturopathy, Unani, Siddha, Sowa Rigpa, and homoeopathy (AYUSH) which functions under the Ministry of AYUSH (MoA). Findings have asserted that during the COVID-19 pandemic a large proportion of the population practiced AYUSH measures across the country and have benefitted considerably.⁵⁵

WHO is working with some research institutions around the world to select traditional medicine products with potential use for the treatment of COVID-19 after being investigated for clinical efficacy and safety. The WHO has been working with countries to ensure the safest and most effective use of traditional medicines, and it will continue to give support in exploring the benefits of traditional medicines. Traditional medicines need to be robustly investigated to avoid putting the lives of people in danger during the period of this pandemic and beyond.⁵⁶

Improving the situation will require both political will and considerable investment in infrastructure, human capacity and new tools.⁵⁷ It needs social and political determination to channelize all the available therapeutic options to win the battle against COVID-19.

CONCLUSION

COVID 19 pandemic has placed the most advanced public health systems into crisis. Countering the ongoing pandemic requires restoring, strengthening and reviewing the current health policies. With the Complementary and alternative medicines gaining momentum in recent years the current health policies are to be revised by integrating complementary medicine with conventional system for curtailing the devastating effects the pandemic worldwide. Bigotry or ignorance cannot be valid reasons to rule out Complementary and alternative medicines as an adjuvant tool in the fight against resurgent epidemics/pandemics. Methodical researches are warranted to further evaluate the efficacy of Complementary and alternative medicines.

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