

Polypharmacy in Times of Covid-19: A Narrative Review

Shreya Gupta^{1*}, Savita Verma²

¹Department of Pharmacology, PGIMER Chandigarh, India;

²Department of Pharmacology, Pt BD Sharma PGIMS Rohtak, Haryana, India

Abstract

COVID-19 pandemic caused by the SARS-Cov-2 virus, has become a serious public health concern worldwide which spread across more than 200 countries in a matter of months. Amidst a deadly second Covid wave in India, the resources and the health infrastructure required to handle the situation was stretched to their limits. Furthermore, due to the non-specific nature of the disease and the plethora of symptoms and complications it presents, the medical management of Covid-19 became complicated and uncertain. Such a grim scenario evokes fear and panic among the citizens, leading to questionable and unnecessary practices such as stocking of medicines, hoarding oxygen cylinders and most importantly, self-medication with over-the-counter drugs, dietary supplements (so-called immune boosters), prescription-only drugs, along with combining the use of alternative systems of medicine. Due to all these reasons, the practice of 'polypharmacy' is becoming rampant among the general population, which in most cases is inappropriate and even harmful. This review summarizes the various patient and physician associated factors promoting polypharmacy, along with examples of the common drugs being prescribed and/or self-administered, and the various steps that can be taken to prevent such futile practices.

Introduction

Covid-19 is a viral disease, caused by SARS-CoV-2 virus, with symptoms ranging from flu-like illness to acute respiratory distress syndrome (ARDS), venous thromboembolism, multi-organ failure, and eventual death. [1] Covid-19 has taken the whole world by storm, with India currently overcoming the heaviest brunt of the pandemic since it began in 2020.

In the deadliest wave yet, India witnessed about 3-4 lakh cases of Covid-19, with over 3000 deaths per day. [2]

It has been over one year since our descent into the pandemic, and we still lack a thorough understanding of all the aspects of this disease, one of the major reasons being the rapid evolution of the virus with multiple mutations and new strains, making not only the management but even the diagnosis tricky and uncertain.

The US CDC has classified 5 Covid strains as variants of concern (VOCs), including the UK, South African, Japanese/Brazilian and Californian strains. [3] Apart from these the 'double mutant or delta', and the 'N440K' variant of COVID-19, which is noted to be behind the unprecedented surge in some states in India, has added to the severity of the disease. [4]

Due to the paucity of well-established evidence-based therapeutics for its prevention and cure, most COVID guidelines advocate a supportive treatment approach, with antivirals, steroids and monoclonal antibodies reserved for moderate-severe disease, with advanced lung involvement and risk of further worsening. [1,5]

However, it is being observed that to a variety of reasons, people are consuming multiple medications, even for mild to moderate cases of COVID-19, most of which are not required, thus leading to inappropriate polypharmacy. [6-8] 'Polypharmacy' as a word in medical science, was first coined about 150 years ago, and is defined as the consumption of 5 or more medicines at a time.

It often is related to the consumption of multiple medicines which may lack scientific grounds, or evidence-based practice. [9,10] While, polypharmacy is discussed more commonly with reference to the at-risk and the elderly population, in the current pandemic it is becoming increasingly evident among all age groups. Data shows that >80% of Covid cases are mild in nature, with

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Gupta S. Polypharmacy in Times of Covid-19: A Narrative Review. AMHSR. 2021;11:1-12

<5% patients progressing onto severe disease and needing ventilator support. [11] Thus, in most Covid cases the use of multiple medicines is irrational, unnecessary, and may even be counter-productive, thereby increasing the risk of adverse events and adding to the patient's financial burden. It becomes important to understand and explain to the patients, the demerits of consuming multiple drugs at once because

such practices can have many short-term and long-term repercussions. [12] This review summarizes the common drugs being consumed and prescribed in India during this pandemic [Table 1]; the various physician and patient associated factors that are promoting polypharmacy in the present-day scenario; the impact that such practices may have on public health, and the various measures that can be taken to curtail it [Table 2].

Table 1: Few examples of drugs being commonly prescribed for COVID-19 in India, along with their ICMR and US-CDC recommendations.

Various Medications Being Prescribed for Covid-19 in India		
Name	Recommendation by ICMR1	Recommendation by US-CDC5
	Antipyretics/analgesics	
Paracetamol	Mild, moderate, severe disease	Mild, moderate, severe disease
NSAIDs	Mild disease	Mild disease
NSAIDs +/- paracetamol fixed drug combinations (FDC)	Not recommended	Not recommended
	Gastrointestinal agents	
Esomeprazole/Omeprazole	Not recommended	Not recommended
Domperidone	Not recommended	Not recommended
Antacids	Not recommended	Not recommended
Probiotics	Not recommended	Not recommended
	Respiratory system agents	
Cough syrup	Mild to moderate disease	
Montelukast + levocetirizine fixed drug combination (FDC)	Not recommended	Not recommended
Antihistaminics (eg. Hydroxyzine)	Not recommended	Not recommended
Betadine/chlorhexidine (for gargles)	Not recommended	Not recommended
	Vitamins/mineral supplements	
Vitamin C tablets	Not recommended	Insufficient data to recommend for/against
Vitamin D tablets	Not recommended	Insufficient data to recommend for/against
Zinc +/- multivitamins	Not recommended	Insufficient data to recommend for/against
Multivitamin capsules/syrup	Mild disease	Insufficient data to recommend for/against
	Antimicrobial agents	
Ivermectin	Mild disease (low certainty of evidence)	Insufficient data to recommend for/against
Hydroxychloroquine	Mild disease (low certainty of evidence)	Not recommended
Favipiravir	Not recommended	Not recommended
Remdesivir	Moderate to severe disease (EUA)	USFDA approved for hospitalised patients
Azithromycin	Moderate to severe (As per antibiogram)	Not recommended unless indicated
Doxycycline	Moderate to severe disease (As per antibiogram)	Not recommended unless indicated
Amoxicillin+clavulanic acid	Moderate to severe disease	Not recommended unless indicated

	(As per antibiogram)	
Cephalosporins	Moderate to severe disease	Not recommended unless indicated
	(As per antibiogram)	
Antifungals (Amphotericin B)	Superimposed mucormycosis	Not recommended unless indicated
	Immunomodulatory agents	
Topical steroids	Not recommended (Superimposed candidiasis only)	Not recommended unless indicated
Inhalational steroids (budesonide)	Mild disease (low certainty of evidence)	Not recommended
Oral steroids (dexamethasone/methylprednisolone)	Moderate disease	Recommended in hospitalised patients who require supplemental Oxygen
Intravenous steroids (dexamethasone/methylprednisolone)	Moderate to severe disease	Recommended in hospitalised patients who require supplemental Oxygen
Tofacitinib	Not recommended	Not recommended
Tocilizumab	Severe disease (EUA)	Recommended in hospitalised patients, requiring oxygen
	Anticoagulants	
Aspirin	Not recommended	Not recommended
Apixaban	Not recommended	Not recommended
Clopidogrel	Not recommended	Not recommended
Enoxaparin injection /Dalteparin injection	Moderate to severe disease	Insufficient data to recommend for/against
	Sedatives/antidepressants/antianxiety agents	
Alprazolam	Not recommended	Not recommended
Zolpidem	Not recommended	Not recommended
Selective Serotonin Reuptake Inhibitors (SSRIs)	Not recommended	Not recommended

Materials & Methods

The literature search for this review was performed by searching various bibliographic databases (Google Scholar, PubMed, and Research Gate).

We principally utilized the articles which were open access, since this research is not funded by any source. The search terms used were: “COVID-19”, “Polypharmacy”, “COVID treatment guidelines”, “Doctor-shopping”, “self-medication”, “steroids”, “multivitamins”, and “public health”, followed by cross-referencing across other reputed journals. Articles with full text and those written in English were included. The latest version of the CDC [5] and ICMR [1] Covid guidelines, as dated prior to the submission of this manuscript have been included.

As this is a narrative review focusing on the current and evolving polypharmacy trends in the Indian scenario, we have included numerous recent newspaper articles, which have helped corroborate our observations with the already prevalent self-medication habits in India, along with providing insight into the current and evolving therapeutic practices. The table listing the examples of drugs being commonly used and abused during Covid pandemic in India was compiled after referencing multiple newspaper and

journal articles, along with the clinical observations of the authors.



Figure 1: Factors Promoting Polypharmacy.

Patient associated factors

The second Covid wave has been brutal, and has stretched the entire health infrastructure to its limits, leading to an acute shortage of resources.

Thus, many people have turned to various unhelpful practices such as stockpiling of medicines and oxygen cylinders, along with rampant use of dietary supplements, antibiotics, antivirals and even steroids, both for therapeutic and prophylactic purposes, without regard or knowledge of the consequences they may face. [13]

Unregulated sale and consumption of dietary supplements: Covid-19 has fortified the community to an important lesson that ‘prevention is better than cure’, but the quest for prevention is making people frantically consume multiple medicines and dietary supplements, thereby promoting the inadvertent practice of polypharmacy during these Covid times. Many of these dietary supplements or nutraceutical such as, vitamins, minerals like zinc, iron etc., herbal supplements like haldi (turmeric) capsules, protein supplements etc. are being consumed left and right, without prescription or doctor’s advice, with the prevailing myth that they act as ‘immune boosters’ and lack any potential side effects even if consumed in large quantities and for long durations. Since the start of the pandemic in 2020, internet has been flooded with a wide range of nutritional information, from a variety of sources on how to prevent or cure COVID-19; however, this information may be confusing and non-evidence-based speculation. [8,14,15]

While, the ICMR guidelines recommend consumption of multivitamins in COVID-19 patients, their exact role in the alteration of disease process is unknown. [1] Renowned doctors all over the country have cautioned against these ‘immune boosters’, stating explicitly that there are no magic pills for boosting immunity, and good diet and adequate sleep is enough for protecting oneself against infectious diseases. [16] Multiple studies [17-23], evaluating the roles of vitamin C, D, zinc and selenium, have been conducted or are ongoing, however, none of the studies conducted so far show prevention or decrease in severity of COVID-19. The US-CDC COVID-19 treatment guidelines [5] also explicitly states that there is insufficient evidence to recommend for or against vitamins C and D, and zinc in the treatment and prevention of COVID-19 [Table 1].

- Other potential risks [17,24] with dietary supplements:
- Intentional/unintentional adulteration or contamination
- Misreporting of the claimed content by manufacturers
- Presence of an undeclared substance
- Deviation from recommended level
- Hypervitaminosis syndrome

The role of zinc was postulated in various studies as an immune booster, but none concluded any significant improvement in the severity and course of the disease. [25-27] Still, zinc was one of the most widely bought and consumed dietary supplement in the pandemic, with people consuming

zinc tablets for months on end. In fact, the role of zinc supplementation is now being evaluated for the spread and increase in severity of mucormycosis, which is an opportunistic fungal infection, now reaching epidemic proportions in India. [28,29] Zinc is required for the life cycle and survival of the fungus, and in vitro studies have evaluated the role of zinc chelators as a treatment option in patients of mucormycosis [30-32].

To summarize, while vitamins, minerals and antioxidants are vital for one’s immune system and various physiological processes, and may be rational for use anemia, protein deficiencies, malnutrition syndromes, eating disorders, malabsorption syndromes, pregnant women, etc.,

It is always preferable to obtain said nutrients from food, rather than from supplements. A healthy and balanced diet can decrease the risk of contracting the infection, and also improve control of diabetes, hypertension, obesity, etc. which are all co-morbidities, adding to the risk of COVID complications.

The key message regarding nutritional supplements is that, while they may be prescribed for Covid positive patients, individuals should not rely on supplements to prevent Covid infection. Irrational and unwarranted consumption of such supplements should be curtailed, and instead one should focus on consuming a healthy diet and exercise regularly.

Self-medication with antimicrobials & steroids in COVID-19: As per the World Health Organization (WHO), self-medication (SM) is the selection and consumption of medicines to treat self-recognized symptoms or ailments without consulting a clinician. [33] It also includes the utilization of previously prescribed or unused drugs, direct purchasing of prescription drugs from pharmacies without consultation, and irrational and recommended usage of over-the-counter (OTC) medicines. [34]

Self-medication habits are particularly common in developing countries, like India, where not only dietary supplements, but even with antibiotics and steroids are sold as OTC drugs, i.e. without a valid prescription. Such practices are a major cause for polypharmacy, since people end up consuming unnecessary medications for prolonged periods. Several studies have been carried out over the years in various parts of India to estimate the prevalence of self-medication habits. In the study conducted by Rajendran et al. [35] In Thrissur municipality, Kerala, in a sample size of 7 [55] adults, it was observed that 3.31% of population practiced self-medication with antibiotics. The most common ailment was sore throat (25%), with azithromycin as the most common antibiotic (39%) self-prescribed for the same. In another study conducted by [36] In Rohtak district of Haryana it was observed that out of 100 households that were interviewed, 73% households practiced self-medication with some or the other class of drugs. Out of the drugs surveyed, the most common classes were analgesics (81%), antacids (44%), and antibiotics (33%), nutritional supplements (23%), cough syrups (16%), antispasmodics (14%), topical applications (34%) and others.

Multiple reports [7,8,38,39] of self-medication practices have been published as newspaper and journal articles from prominent hospitals across India, citing incidences where patients land up in complications after consuming the so-called ‘popular’ or ‘known Covid drugs’ like ivermectin, hydroxychloroquine, doxycycline and dexamethasone, to ‘prevent severe disease’. The vast pool of knowledge available online, through news or social media is becoming a major factor in spreading misconceptions about all these drugs. They have several contraindications and warnings, and are leading on to complications at a later stage, which are adding to the burden of an already saturated healthcare infrastructure.

Presently, many people are self-medicating with broad spectrum antibiotics like azithromycin, cephalosporins, doxycycline etc. right from day 1 of fever onset, without even getting themselves tested for Covid or waiting for experts’ recommendation. They end up consuming these prescription drugs (often sold as over-the-counter medications in India), for days or weeks on end, without regard to their indication or adverse effects. This is also a major factor contributing further to the spread of antimicrobial resistance, which is already a major public health concern. [7,39,40]

Antivirals like favipiravir and Remdesivir are being used for mild-moderate and moderate-severe Covid infection, respectively. While, Remdesivir requires intravenous administration and under close monitoring in hospital settings¹, favipiravir is being marketed as oral tablets and is readily available. So, self-medication with favipiravir is also common, with patients procuring the same directly from pharmacists, even though its approval mandates a prescription from a registered medical practitioner. [8]

However, the most dangerous example of self-medication is the consumption of steroids. Doctors have repeatedly warned against the use of steroids without medical consultation because they have a plethora of short-term and long-term side effects, and are only to be taken under specific conditions, and under strict supervision of the consulting physician. [41-43] Multiple case reports and newspaper reports are available describing a variety of complications and deterioration of patients’ condition because they began self-administering steroids in the early stages of illness and/or without medical advice. [44-46] Besides suppressing one’s immune system, some common risks of steroid consumption include, weight gain, fluid retention, hormonal imbalance, anxiety and disturbed sleep, while some uncommon and dangerous complications include hemorrhagic events, visual defects, uncontrolled diabetes, reactivation of latent infections and opportunistic infections like candidiasis and mucormycosis. [43]

As per the ICMR guidelines¹, oral steroids are indicated only in moderate or severe cases, with the possibility of further deterioration as it becomes crucial to balance pro- and anti-inflammatory mediators, to curtail multi-organ damage (specifically lung fibrosis), and/or prevent cytokine storm.

Prescription-Sharing Practices: Another common practice involving self-medication, is sharing of prescriptions among patients, via social media (e.g. Whatsapp) or telephonically. The sudden rise in cases during the second wave of Covid-19 has led to an acute shortage of resources, including long waiting periods for RT-PCR testing and delays in booking tele-consultation appointments. [47,48] Due to all these issues some people are preferring to skip getting themselves tested, assuming they have Covid, and are straightaway starting medications by borrowing someone else’s prescription or using the ones being circulated on social media, many of which are fake.

Mental health issues due to COVID-19 pandemic: The concept of health is incomplete without taking one’s mental health into consideration. In fact, mental health is still one of the most neglected and undertreated healthcare concerns in the present-day scenario, especially owing to the dire effects of the current pandemic adversely affecting the psychological profile of most, if not all individuals. The anxiety of contracting Covid is multiplied manifold by the isolation norms, social distancing, lockdown/curfew measures, closure of educational institutes, workplaces, lack of entertainment options, travel ban, etc. All of these measures, along with the grief and fear of losing one’s life or that of someone close, are all playing havoc on the mental and social health of people worldwide, and have led to additional problems such as generalized anxiety disorder, depression, insomnia, panic attacks etc., for which long term medications are now being prescribed or are more frequently being self-consumed against the better judgment of the medical fraternity. [49,50] The most common self-employed strategies include alcohol consumption, nicotine, recreational drugs like marijuana, amphetamines etc., and prescription medicines like pain killers, including NSAIDs and opioids. In a cross-sectional study conducted by [51], online survey was carried out using self-rating anxiety scale, validated Covid-19 Anxiety Inventory Items and self-medication practices during COVID-19 pandemic. Out of 1100 responses received, prevalence of mild-to-moderate, moderate-to-severe, and severe anxiety cases were 23.1%, 4.7%, and 0.54%, respectively. Among the most commonly reported self-medications were with NSAIDs, anti-ulcer drugs, anti-histaminic and benzodiazepines.

Doctor Shopping’ in India: Another unique practice in our country is that of ‘doctor shopping’, which is the tendency of patients to receive care from multiple doctors. Since India lacks the referral system in healthcare, one patient can visit numerous doctors, of same/different specialties, for the same illness. [52] There exists a lack of trust between the patient and physician on most occasions, which leads them to consult multiple doctors. This is becoming very common in Covid times, also because remote or tele-consultation services make it easier for one patient to confer with multiple physicians, and as a result they end up with multiple prescriptions. While, it is any patient’s right to take different opinions, especially in a high panic state like the current pandemic, the old saying that too many cooks spoil the broth,

holds true in such a scenario. This is because, consulting multiple physicians creates more confusion and it not only promotes polypharmacy but can also lead to repetition or increase/decrease in the dose and frequency of same medicine, which lead to over/under dosage, adding to side effect profile and toxicity of the drugs. [53]

Since there is a wide clinical spectrum for Covid illness, every case has to be handled differently, keeping in mind co-morbidities, age, previous drug intake, severity, etc. Besides, every clinician has a unique approach to medical management, based on their knowledge and experience. Even if a second opinion is warranted it should be taken only on physician's referral, from a senior doctor, who may be more experienced and/or a specialist, like a pulmonologist. Also, since the present healthcare infrastructure is already overwhelmed, with over-burdened doctors and hospitals running on full capacity, it becomes extremely wasteful to unnecessarily utilize resources and most importantly waste money and time on such a practice like 'doctor shopping'.

Physician associated factors

Due to the wide spectrum of Covid-19, targeting multiple organ systems and physiological processes, physicians have to keep a broad perspective, and adopt a multi-system approach to tackle the infection. The Covid treatment guidelines [1,5,54] are still evolving, with minor and major changes happening every few months. It becomes tough for physicians to keep up with this overload of information, when they are already heavily burdened with patient care.

Also, since many patients present with co-morbidities which are known to worsen due to covid-19, or they may add to the severity of Covid illness, so along with supportive measures and symptomatic treatment, most patients now require additional drugs such as, anti-coagulants, steroids, insulin etc., thus leading to unavoidable polypharmacy.

However, irrational prescriptions are still one of the major causes of polypharmacy and there are many situations in which multiple medicines are not needed, and their unreasonable use can be prevented.

With respect to dietary supplements, no vitamin or mineral has so far shown any concrete evidence for prevention or cure of Covid-19, hence, their widespread prescription and use, lacks scientific basis. Without consideration of the micronutrient requirements of the patient, multivitamins, vitamin C, vitamin D and zinc are being prescribed all at once, when none of these micronutrients have any well-defined roles in the treatment of covid-19 so far.

The latest ICMR/AIIMS guidelines [1] clearly specify that antibiotics are only to be used in Covid management, if there exists a clear indication of a superimposed bacterial infection. However, most physicians are prescribing azithromycin, doxycycline, amoxicillin, cephalosporin's, etc., even in mild cases, having no indication of bacterial infection at all. [55,56] This practice can rapidly lead to the worsening of antibiotic resistance, and if not curtailed, we might be

looking at a bacterial pandemic next, which may prove to be much more devastating, than the viral pandemic we currently face.

Apart from antibiotics, antivirals also have a limited role so far, with definite evidence of their benefits still lacking. Remdesivir has been approved by the USFDA for Covid-19, but in India it is still under emergency use authorization (EUA) by the Drugs Controller General of India (DCGI), citing lack of sufficient evidence for its full approval. It is only to be prescribed in selected moderate-severe hospitalized Covid patients, receiving supplemental oxygen and is to be prescribed within 10 days of disease onset. Favipiravir, on the other hand has not received any reference in ICMR1, CGHS54, or US-CDC5 guidelines and is currently being used as an off-label oral therapy for mild to moderate Covid cases, after marketing approval by the DCGI, in June 2020; however, unequivocal role of favipiravir is still largely lacking. Hence, antivirals such as favipiravir and Remdesivir should be used only if the situation mandates, as per the Covid guidelines, with continuous monitoring of the patient, and should not be prescribed indiscriminately.

Similarly, while inhalational steroids are now indicated for mild Covid cases [1,54] systemic steroids are to be used judiciously and with great caution, since their misuse can lead to multiple side effects, including opportunistic infections like candidiasis and mucormycosis. [45,46] Steroids are considered as life-saving drugs for severe cases of Covid, but they should be considered as a double-edged sword, especially if their timing, dosage or duration is wrongly determined.

Impact of Polypharmacy

Consuming numerous medicines at once may be a necessary evil for some, especially those suffering from multiple illnesses and those having long term sequel, but in these uncertain times, it is important for us to understand the implications of, and curtail the practice of inappropriate polypharmacy. [55]

Some schools of thought refer to polypharmacy as a part of potentially inappropriate prescribing (PIP), which in turn may cause adverse clinical outcomes due to multiple drug interactions and side effects, all of which eventually leads to worsening of one's condition and increased healthcare costs. [57]

Multiple drug intakes are a major risk factor for drug-drug, drug-food and drug-disease interactions, all of which are important to know and suspect timely. [12] Physicians should take a detailed history of the various medications being consumed by the patient (allopathic, homeopathic, Ayurveda, etc.), their dose, duration and route of administration, along with any co-morbidities, drug allergies, history of substance abuse, etc., all of which need to be correlated with one's Covid positive diagnosis; identifying and amending any predisposing factors that may lead to further complications and/or add to the severity of the infection. This also why

patients should never take medicines (including dietary supplements), without a proper prescription, and disclose any and all medications they may have consumed on their own.

Each individual is unique and has varied metabolism and dietary requirements. Hence, although vitamin supplements may be indicated during the course of Covid-19, as per ICMR guidelines¹, but they are usually not required unconditionally or for prolonged duration. One of the reasons for indiscriminate use of vitamins is their easy availability, and the myth that they do not cause harm, but this is not true. Hypervitaminosis is an entity that is described due to over consumption of vitamin supplements.^[58] Vitamin C is being widely promoted as an immunity booster, but excess intake may cause gastric upset, nausea, kidney stones and disrupt antioxidant balance of the body. Vitamin D toxicity can lead to seizures, depression, dental problems, brittle bones etc. Excess vitamin K can lead to thrombi formation as it plays a vital role in blood clotting. Likewise, other vitamins can also have detrimental effects on one's health if not taken as per the body's requirement.^[58,59] In fact, indiscriminate use of zinc is now being implicated as one of the contributing factors for mucormycosis, even in recovered patients of Covid-19.^[29,31]

Another pressing concern is the emergence of antibacterial resistance (AMR), which is already rampant worldwide, and is being overlooked in the Covid pandemic, owing to the indiscriminate use of broad-spectrum antibiotics like azithromycin by patients and physicians alike. It is vital for everyone to understand that antibiotics are not to be taken in any undetermined bacterial infection, and are definitely not indicated prophylactically for mild Covid infection.^[39,40]

Conclusion

Covid-19 has a complex clinical spectrum, to say the least. It has been almost 2 years since it first began, and our knowledge of its prevention, management and prognosis is still evolving. Numerous medications have been tried and are undergoing trials for the same, but no drug has emerged as first-line, or treatment-of-choice for covid-19. All these uncertainties and limitations have resorted both patients and physicians, to the habit of consuming and prescribing multiple drugs, respectively, leading to the inadvertent practice of polypharmacy. Notwithstanding the glaring absence of clear evidence of clinical efficacy and safety, broad spectrum antibiotics and dietary supplements are widely being used as off-label therapies for prophylaxis and treatment of Covid-19. The rationale behind their prescription is still obscure, and their widespread use is at odds with rational pharmacotherapeutics, which is the cornerstone of the principles of pharmacotherapy, as first advised by the World Health Organization (WHO) back in 1985.^[60]

Thus, mindlessly consuming or prescribing medicines is never the solution or the cure. Dubious practices such as, self-medication, prescription-sharing, doctor-shopping, etc. must be discouraged. Physicians also must be extremely

cautious of what drugs they advise in these uncertain times, and must individualize prescriptions as per patient condition, severity, co-morbidities and clinical history.

References

1. Clinical Management Protocol for Covid-19 (In Adults).
2. India. Worldometer. (n.d.).
3. Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention.
4. Kadidal A. Second Covid-19 wave in Karnataka largely driven by Delta variant, say experts. Deccan Herald. 2021.
5. COVID-19 Treatment Guidelines Panel. Coronavirus Disease (COVID-19) Treatment Guidelines. National Institutes of Health. 2019.
6. Iyer M. Government's new Covid prescription drops many 'common' drugs. The Times of India. 2019.
7. Maya C. Explained Why has doctors cautioned against misuse of CT scans and steroids to diagnose and treat COVID-19? The Hindu. 2021.
8. Chandna H. 'Fearing Covid', Indians are popping ivermectin, HCQ, dexamethasone all self-prescribed. The Print. 2021
9. Friend DG. Polypharmacy; multiple-ingredient and shotgun prescriptions. N Engl J Med. 1959; 260:1015–1018.
10. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr. 2017; 17:230.
11. Staff FP. COVID is a mild disease, less than 5% of patients need ventilator, says AIIMS chief Randeep Guleria. Firstpost. 2021.
12. Halli-Tierney AD, Scarbrough C, Carroll D. Polypharmacy: evaluating risks and deprescribing. American family physician. 2019; 100:32-38.
13. F. India's Covid-19 shortages spur black market for drugs, oxygen. France 24. 2021.
14. Desai S. Must-have immunity boosters in your daily nutrition - Times of India. The Times of India. 2021.
15. Online FE. Coronavirus: Rise in demand for immunity boosters amidst the pandemic. 2020.
16. Sunitha RR. Good sleep, not popping pills, aids immunity: Bengaluru doctors. The Times of India. 2020.
17. De Faria Coelho-Ravagnani C, Corgosinho FC, Sanches FL, Prado CM, Laviano A, Mota JF, et al. Dietary recommendations during the COVID-19 pandemic. Nutrition Reviews. 2021; 79:382-393.
18. Wei XB, Wang ZH, Liao XL, et al. Efficacy of vitamin C in patients with sepsis: an updated meta-analysis. Eur J Pharmacol. 2020; 868:172889.
19. Thomas S, Patel D, Bittel B. Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 infection: the COVID A to Z randomized clinical trial. JAMA Netw Open. 2021; 4:e210369.
20. Zhang J, Rao X, Li Y. Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. Ann Intensive Care. 2021; 11:5.
21. Fowler AA, Syed AA, Knowlson S. Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis. J Transl Med. 2014; 12:32.
22. Aranow C. Vitamin D and the immune system. J Investig Med. 2011; 59:881-886.

23. Fisher SA, Rahimzadeh M, Brierley C. The role of vitamin D in increasing circulating T regulatory cell numbers and modulating T regulatory cell phenotypes in patients with inflammatory disease or in healthy volunteers: a systematic review. *PLoS One*. 2019; 14:e0222313.
24. Adams KK, Baker WL, Sobieraj DM. Myth Busters: Dietary Supplements and COVID-19. *Ann Pharmacother*. 2020; 54:820-826.
25. Thomas S, Patel Debited B. Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 Infection: the COVID a to z randomized clinical trial. *JAMA Netw Open*. 2021; 4:e210369.
26. Yao JS, Paguio JA, Dee EC. The minimal effect of zinc on the survival of hospitalized patients with COVID-19: an observational study. *Chest*. 2021; 159:108-111.
27. Frontera JA, Rahimian JO, Yaghi S. Treatment with zinc is associated with reduced in-hospital mortality among COVID-19 patients: a multi-center cohort study. *Res Sq*. 2020.
28. I. Zinc use linked to black fungus but more research needed: Experts. *The Pioneer*.
29. Iyer M. Zinc overuse driving black fungus epidemic within pandemic? Doctors want study. *The Times of India*. 2021.
30. Leonardelli F, Macedo D, Dudiuk C, Theill L, Cabeza MS, Gamarra S, Garcia-Effron G. In Vitro Activity of Combinations of Zinc Chelators with Amphotericin B and Posaconazole against Six Mucorales Species. *Antimicrob Agents Chemother*. 2019;63:e00266-19.
31. Wilson D. An evolutionary perspective on zinc uptake by human fungal pathogens. *Metallomics*. 2015;7:979-985.
32. Zhou J. Zn biosorption by *Rhizopus arrhizus* and other fungi. *Appl Microbiol Biotechnol*. 1999; 51: 686–693.
33. World Health Organization. Guidelines for the regulatory assessment of medicinal products for use in self-medication. Geneva: World Health Organization; 2000.
34. Eticha T, Mesfin K. Self-medication practices in Mekelle, Ethiopia. *PLoS One*. 2014; 9:e97464.
35. Rajendran A, Kulirankal KG, Rakesh PS, George S. Prevalence and pattern of antibiotic self-medication practice in an urban population of Kerala, India: A cross-sectional study. *Indian J Community Med* 2019;44:42-45.
36. Kaushal J, Gupta MC, Jindal P, Verma S. Self-medication patterns and drug use behavior in housewives belonging to the middle income group in a city in northern India. *Indian J Community Med*. 2012;37:16-19.
37. Molento MB. COVID-19 and the rush for self-medication and self-dosing with ivermectin: A word of caution. *One Health*. 2020; 10:100148.
38. Patil AD, Sharma H, Tatarbe T. COVID-19 and concerns related to self-medication. *Int J Basic Clin Pharmacol*. 2020;9:1475-1476.
39. B. Antibiotics for Covid patients worsen India's superbug plight. 2021.
40. Zhang A, Hobman EV, De Barro P, Young A, Carter DJ, Byrne M, et al. Self-Medication with Antibiotics for Protection against COVID-19: The Role of Psychological Distress, Knowledge of, and Experiences with Antibiotics. *Antibiotics (Basel)*. 2021;10:232.
41. Veronese N, Demurtas J, Yang L. Use of corticosteroids in coronavirus disease 2019 pneumonia: a systematic review of the literature. *Front Med* 2020;7:170.
42. Arora K, Panda PK. Steroid harms if given early in COVID-19 viraemia. *BMJ Case Reports CP*. 2021;14:e241105.
43. Noreen S, Maqbool I, Madni A. Dexamethasone: Therapeutic potential, risks, and future projection during COVID-19 pandemic. *European journal of pharmacology*. 2021;8:173854.
44. Chari B. Goa doctors cite risks of steroid abuse by Covid patients. *The Times of India*. 2014.
45. A. Misuse Of Steroids A Major Cause Of Black Fungus, Says AIIMS Chief. *NDTV.Com*. 2021.
46. Steroid misuse in COVID-19 patients can cause life threatening infections. *Down-to-earth*. 2021.
47. Didyala A. Covid-19: Social media prescriptions the new headache. *The Times of India*. 2021.
48. P. Self-medication with borrowed prescriptions adding to COVID-19 crisis, say doctors. *The Economic Times*. 2020.
49. Mental health and COVID-19. *WHO*. 2021.
50. Moukaddam N, Shah A. Psychiatrists beware! The impact of COVID-19 and pandemics on mental health. *Psychiatric Times* 2020.
51. Chopra D, Bhandari B, Sidhu JK, Jakhar K, Jamil F, Gupta R, et al. Prevalence of self-reported anxiety and self-medication among upper and middle socioeconomic strata amidst COVID-19 pandemic. *J Edu Health Promot*. 2021; 10:73.
52. Andhale S. Doctor shopping the new trend among patients. *DNA India*. 2015.
53. Biernikiewicz M, Taieb V, Toumi M. Characteristics of doctor-shoppers: a systematic literature review. *J Mark Access Health Policy*. 2019;7:1595953.
54. Comprehensive Guidelines for Management of COVID-19 patients. 2021.
55. Study adds more evidence of antibiotic overuse in COVID-19 patients. 2021.
56. Manohar P, Loh B, Leptihn S. Will the Overuse of Antibiotics During the Coronavirus Pandemic Accelerate Antimicrobial Resistance of Bacteria?.
57. Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K, et al. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. *Br J Clin Pharmacol*. 2010;69:543-552.
58. Sadadekar A. Vitamins are Vital! Experts warn against Hypervitaminosis. *Times Now*. 2020.
59. Roop JK. Hypervitaminosis - an emerging pathological condition. *Int J Health Sci Res*. 2018; 8:280-288.
60. WHO. The Pursuit of Responsible Use of Medicines. 2012.