Indian Journal of Natural Products and Resources
Vol. 15(2), June 2024, pp. 313-320
DOI: 10.56042/ijnpr.v15i2.11504

Treatment modalities of home isolated COVID-19 patients in India: Lessons learnt

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Received 24 April 2024; revised received 05 June 2024; accepted 06 June 2024

This study investigated the treatment modalities that medical practitioners in India followed for home-isolated patients. The responses via web-based survey from 201 medical practitioners treating more than 11000 COVID-19 patients, fulfilling the inclusion criteria, were analysed using STATA 11. Furthermore, we have also compared the treatment modalities followed by doctors in government and private setups. Doctors from both set up recommended protein diets followed by liquids, fruits and vegetables. Interestingly, 61.1% of government doctors advised COVID-19 treatment based on symptoms alone without an RT-PCR test, in contrast to private practitioners (38.9%). Around 45% of doctors advised blood anticoagulants to their patients. Among the various drugs, oral steroids and fabiflu prescriptions were predominantly preferred by private doctors in comparison to government doctors who preferred giving antibiotics for treatment. The present study reflects the doctors' zest to contain and cure the COVID-19 disease through their best-understood management regime guided by experience and laid guidelines to deify the suddenness of this pandemic and uphold human life, yet retrospectively, usage of drugs still needs to be established in the light of science through trials and evidence.

Keywords: COVID-19 management, COVID-19, Home isolation, Medical practitioners, Treatment modality

IPC code; Int. cl. (2021.01)– A61

Introduction

Since COVID-19's emergence in December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly advanced as a major global pandemic[1]. Threatening 220 countries with currently 672 million reported cases, and it has resulted in more than four million lost lives across the globe[2]. Measures taken to contain the spread of the virus by imposing restrictions on movement brought economic activities to a practical standstill and pushed the world into a deeper recession, from one peril to another[3]. Thus, the agenda was to curb the infection; hence, many therapeutics guidelines emerged, ranging from vitamins, zinc, antibiotics, antivirals and glucocorticoids to passive immunisation with convalescent plasma therapy and monoclonal antibodies, many of which have been retracted too[4,5]. This included active immunisation for prevention and to attain immunity.

However, COVID-19 was marked with a majority of asymptomatic cases, with 80% of cases having mild symptoms[4-6]. Such cases typically recovered with minimal interventions and were managed by isolating patients at home with proper medical supervision. Ministry of Health & Family Welfare (MoHFW), India, has thus issued and updated guidelines for home isolation (HI) from time to time to clarify selection criteria, precautions that need to be followed by such patients and their families, signs that require monitoring and prompt reporting to health workers[4]. While a patient was allowed HI, all other family members, including other contacts, followed the home quarantine guidelines as given by MoHFW[5].

The survey aims to understand the treatment modalities followed by doctors in India for home-isolated COVID-19 patients (HICPs), especially when

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Supplementary tables are available online only.

the scientific world was still struggling to understand the treatment process itself given the suddenness of the pandemic and lack of strong evidence from clinical trials about improved outcomes/decline in of mortality rate or knowledge of basic prophylactic treatment. Further, with the paucity of information on viruses and therapeutic options, it is imminent that treatment modalities followed by various doctors in the country be compared. In fact, many countries adhered to guidelines issued by the World Health Organization (WHO) or to their country's health department directives[6]. Therefore, an insight into the regime of drugs and treatment modalities by doctors (private and government) would assess the choice and variations of the therapeutic regime. It will provide action and knowledge inputs for further such outbreaks and together lay the foundations for policy guidelines in any such emergent situations. Thus, we were urged to compare distinct methods and procedures followed by different doctors or COVID-19 frontline workers for HICPs. The survey of 201 doctors treating more than 11000 patients aims to provide insight into the comparison of detection techniques, diet recommendations, drugs, steroids and antibiotics administered by the doctors.

Materials and Methods

Data source

A two-step validated questionnaire was designed, first by a pilot study using 20 volunteers, which was altered based on the inputs, and again, 20 volunteers from the medical fraternity were recruited for validation of the questionnaire. Approval was obtained from the institutional ethics committee for the validated questionnaire used to conduct the retrospective study.

Inclusion criteria

The survey was administered to subjects of India who were registered doctors during COVID-19 and with informed consent.

Exclusion criteria

Subjects (doctors) who were not registered or non-residents of India and did not provided the complete details in the form were excluded.

The questionnaire encompasses the social and demographic profiles of the doctors who administered therapy to patients suffering from COVID-19 in India, detection mode, diet recommendations, prophylactic `measures, drugs, steroids and antibiotics administered by them. The survey was conducted from June 1 to July 31, 2021, through an online Google form. The link to the Google survey form was shared with the doctors of authors, co-authors, friends, family members and relatives through emails, WhatsApp, and Facebook. Doctors were requested to share the questionnaire with their medical colleagues to increase the number of responses to the online survey. The data collected was a mix of doctors from government and private setups.

Data analysis

A total of 210 doctors from India participated in the online survey. After the exclusion of 9 responses with insufficient information, the remaining 201 responses were analysed. Descriptive analyses were used for socio-demographic and categorical data. Chi-square and Fisher's exact tests were performed by GraphPad Prism 5 to obtain the *p*-value and determine the significance.

Results

Data from 201 doctors from government and private setup who had treated more than eleven thousand home-isolated COVID-19 Patients (HICPs) were included, as shown in the flow chart (Fig. 1). Out of a total of 201 doctors, 48.3% (n=97) belonged to government hospitals and 51.7% (n=104) belonged to private hospitals.

Demographic details of doctors

Overall, 201 doctors (mean age of 38.8±9.8) from government and private hospitals who have treated more than eleven thousand HICPs were enrolled in the study, of which 98 (48.8%) were females, and 103 (51.2%) were males (Supplementary Table 1). The enrolled doctors were predominantly from Northern India (n=186; 92.5%), followed by other parts of India. In addition, the median range of HICPs was 50 (25-200), whom the doctors treated.

Regime of diet, prophylactic measures and blood tests recommended to HICPs by doctors in government and private setup

The overall regime was observed to be the same whether the doctors belonged to a government or private hospitals. There was no significant difference in the diet recommended to HICP, as doctors from both set up recommended protein diets followed by liquids, fruits and vegetables (Supplementary Table 2). In addition, as prophylactic measures, 93.03% of doctors advised the patients to do breathing

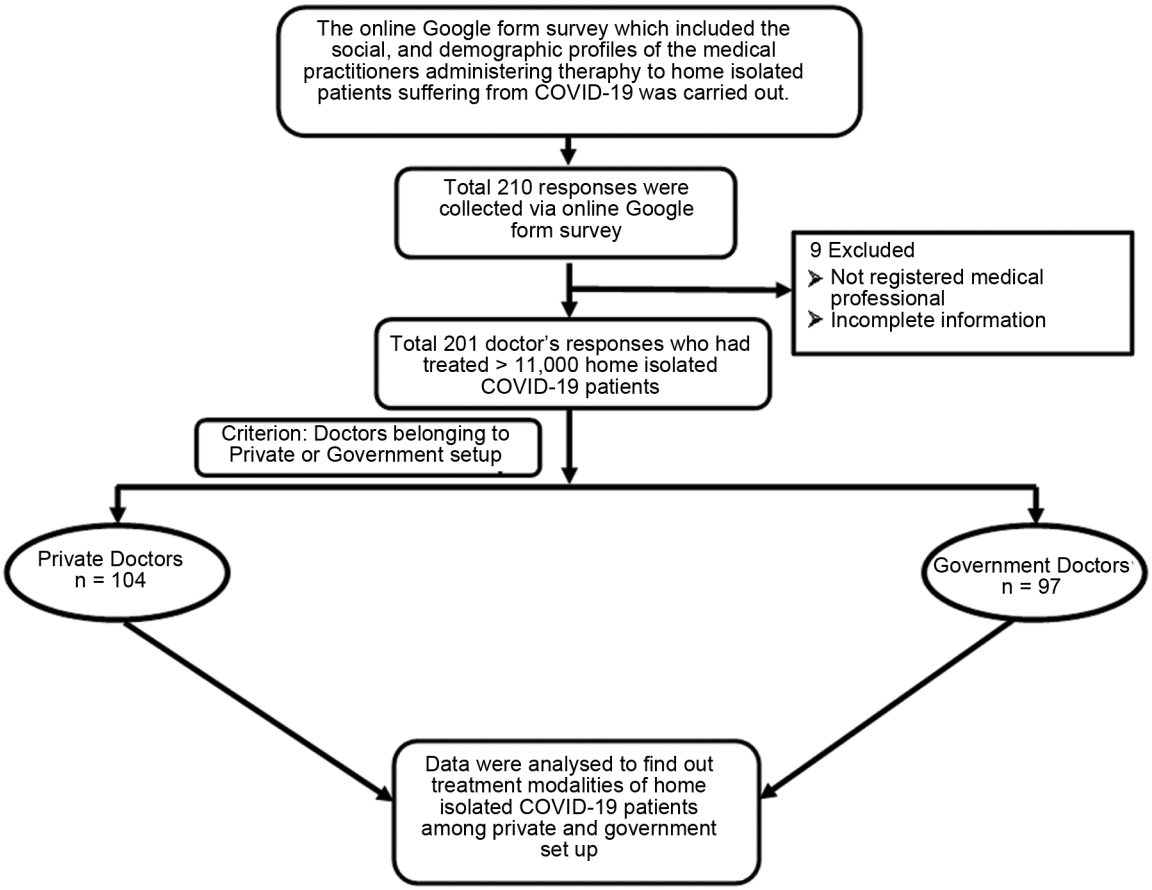

Fig. 1 — Flow chart showing recruitment of medical professionals in the survey "Treatment Modalities of Home Isolated COVID-19 Patients in India".

exercises, and 88.5% encouraged them to wear a mask at home. Around 76.8% of doctors advised for home isolation (HI) of 14 days. More than half of doctors (56.34%) advised the patients to a complete blood test after 5 days of sickness, followed by 40% of doctors who advised after 3 days, and only 22% of doctors advised an immediate test (Supplementary Table 2). Intriguingly, the reverse transcription-polymerase chain reaction (RT-PCR) test was advised maximum by 92.04% of doctors to their HICPs as compared to rapid (10%) and another radiological test (6%).

Comparative spectrum of clinical symptoms of HICP presented (n= > 11,000) to doctors

Among the COVID-19 symptoms, fever was the most prevalent symptom. However, other symptoms were manifested in the following order of frequency such as dry cough>sorethroat> tiredness> loss of smell/taste>difficulty in breathing> headache>diarrhoea>vomiting, among patients (Fig. 2). In addition, body ache and loss of appetite were the least reported symptoms.

Comparison of treatment advised to HICPs

Interestingly, around 61.1% of government doctors advised treatment to HICPs based on their symptoms without a viral diagnosis, in contrast to 38.9% private doctors (Fig. 3a). Further, because of the worsening oxygen saturation, the majority of HICPs were advised computed tomography (CT) by doctors of private hospitals, in comparison to government doctors. Contrastingly, the majority of patients having chronic or intractable coughs were advised for CT by government doctors rather than private doctors (Fig. 3b).

Furthermore, around 45% of doctors advised blood thinners to HICP. Among different available blood thinners, 50% of the doctor's choice was ecosprin (Fig. 3c). Among the various treatments by doctors, the most prevalent was vitamin C, zinc followed by vitamin D3 (Fig. 3d). Likewise, ivermectin was also

advised by 60% of doctors to their patients. The antibiotics prescribed were azithromycin and doxycycline as supportive antibacterial therapy. Strangely, azithromycin was the drug of choice by doctors in government setup and doxycycline was favoured by doctors in private setup (Fig. 3e). However, government doctors significantly (P<0.05) prescribed antibiotics more than private ones. On the contrary, oral steroid prescriptions were predominantly preferred by private doctors over government professionals. The choice of oral steroids was in the order of methylprednisolone> prednisolone 40 mg>dexamethasone> hydrocortisone 60 mg (Fig. 3e). Notably, fabiflu was predominantly advised as antiviral by the doctors, though the number of them prescribing was less (56.4%) as compared to antibiotics and steroids. Paracetamol was given as antipyretic by 10.1% of doctors, while hydroxychloroquine (HCQS) was chosen only by 14.9% of doctors as an antiviral (Fig. 3d).

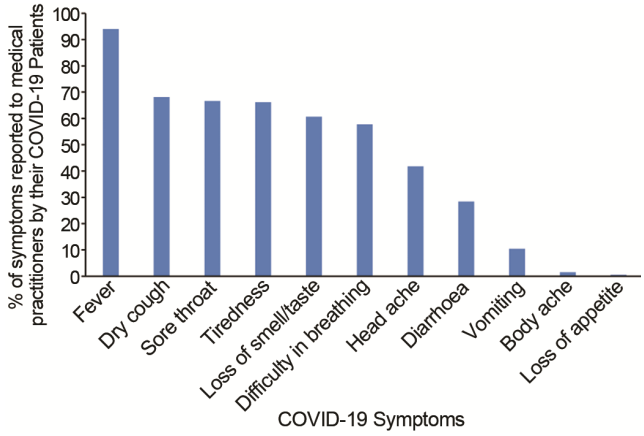

Fig. 2 — Comparative spectrum of clinical symptoms of home-isolated COVID-19 patients (n= > 11,000) reported to the Indian medical practitioners.

Discussion

Due to the absence of effective vaccination against COVID-19 during the second wave, the major impetus was to repurpose existing multipronged therapies or drugs to combat this novel coronavirus.

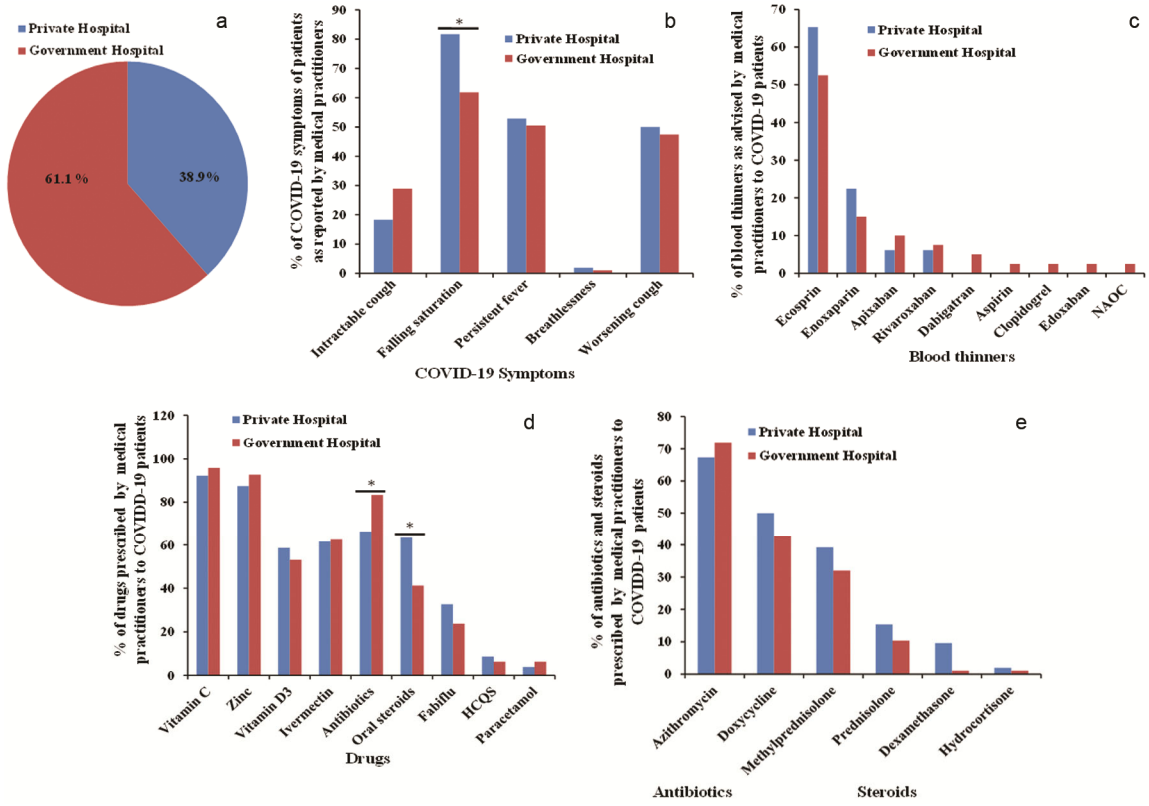

Fig. 3 — Comparison of treatment advised to COVID-19 patients by various Indian medical professionals in government and private setup. a) Comparative percentage of doctors of different hospitals (government and private) who advised treatment without RT-PCR confirmation of COVID-19 (n=9, out of 201); b) Comparative percentage of different doctors of hospitals (government and private) who advised CT based on symptoms; c) Comparative percentage of doctors of different hospitals (government and private) who advised blood thinners to COVID-19 patients; d) Comparative percentage of doctors of different hospitals (government and private) who advised treatment/drugs; and e) Comparative percentage of doctors of different hospitals (government and private) who advised different antibiotics and steroids. Significance P<0.05 among the groups represented by *

Therefore, many guidelines were recommended by state and global healthcare institutes to ensure that healthcare providers, patients, and policy advisors have uniform treatment and optimum management of COVID-19. The MoHFW of India published guidelines for HICP and instructions for their family as early as 24th May 2021, which was revised many times[6]. In this given ambience without valid drugs with clinical trials, it becomes imperative to study how far our healthcare providers conform to the guidelines or did they venture out for new modalities to fit in the demographic human variation. Therefore, in the present study, we have evaluated various therapeutic regimes that have been used to treat HICP (>11,000) by doctors belonging to both private and government set up.

Irrespective of different available diagnostic tests, the detection of infection by nasopharyngeal swab specimens using RT-PCR tests guided by WHO was used as a gold standard for diagnosing SARS-CoV-2 infection. This was the only test therein which, if performed correctly, was sensitive and specific to detect the infection[7]. Furthermore, 70.64% of doctors advised blood parameters profiling on the day of diagnosis following the ambient practice in the world, and again after five days of diagnosis because there would be more chances to knock out cytokine storm between the 8th to 12th day, also known as a critical period[8]. The variation in blood parameters over a period of time was predictive in the progression of disease and detection of cytokine storm if any, which causes an aggressive inflammatory response in COVID-19 patients. Irrespective of diverse COVID-19 symptoms among HICP blood profiling tests were made mandatory by the government and strictly adhered by doctors[8].

Doctors (private and government) also advised breathing exercises to almost all patients because deep breathing and forced cough strengthen the lung muscles, and assist in the clearing of mucus from respiratory tract respectively. However, these exercises were ineffective in patients with dry cough[9]. Moreover, patients were advised prophylactic measures such as wearing a mask and staying in quarantine for 14 days to prevent respiratory SARS-CoV-2 transmission and dissemination to non-infectious person (recommended by WHO) regardless of having asymptomatic or symptomatic COVID-19 infection[10].

In the present study, symptoms reported by HICP to their doctor were fever, dry cough, sore throat, tiredness, loss of smell/taste, difficulty in breathing, headache, diarrhoea and vomiting in resonation with the reported literature[11,12]. In corroboration with the present study, Guan *et al.* reported that the most common symptoms of COVID-19 in China were fever (43.8% on admission and 88.7% during hospitalisation) and cough (67.8%)[11]. However, in comparison to the present study, another retrospective study on isolated home COVID-19 patients in Istanbul city reported cough as the most frequent symptoms followed by shortness of breath[12].

Once the infection was diagnosed, doctors recommended nutritional therapy along with drugs and other treatment. Since HICPs had mild symptoms, the first line of treatment was nutritional therapy to boost the immune system, consequently leading to speedy and complete recovery of patients[13]. Also, several natural bioactive compounds aid in reducing inflammatory response as they have a tendency to bind with the angiotensin-converting enzyme 2 (ACE2) receptor which is an entryway for SARS-CoV-2[13]. In addition, a study demonstrated the importance of adequate or good nutritional status in recovering the clinical outcome of patients[14]. The present study showed that doctors (n= 61%) recommended diet regimes rich in protein, fruits, vegetables and liquids for HICP. The reported literature also confirms that proteins are required for COVID-19 patients as their catabolism is driven by inflammatory mediators, although the quantity of protein intake or any other diet required to be adjusted with nutritional status and disease severity[15,16].

Further, the study investigated the treatment modalities advised to HICPs. Overall, 80% of doctors advised blood tests. Around 61.1% of government doctors advised treatment for COVID-19 without any confirmed viral diagnosis in contrast to private doctors. Thus, in more than half of the cases, medical treatment was not subjected to confirmed COVID-19 diagnosis due to the over burdening of patients in government hospitals forcing doctors to advise treatment based on the symptoms rather than RT-PCR reports. Moreover, the non-reliability of the RT-PCR (not 100% accurate) test showed that patients with COVID-19 symptoms such as breathing difficulty often showed negative RT-PCR results[17].

WHO suggested the use of pulse oximetry to monitor the level of oxygen in the blood of HICPs[18]. Falling levels of oxygen saturation were an alert to shift the patient to proper hospital care. CT scan was also an important investigation to ascertain the status

of lungs in HICPs. In our study, doctors recommended CT to those HICPs who had worse oxygen saturation. The frequency of recommending CT scans was found to be significantly higher by private doctors than by government doctors. One of the reasons may be that 99% of CT scan diagnostics laboratories are private and expensive, and CT scans represent viral pneumonia, which is a strong indicator of COVID-19 infection compared to RT-PCR.

As reported by the National Institutes of Health (NIH), USA, patients did develop blood clots due to high inflammation leading to serious health complications; therefore, blood thinners helped in reducing the death rate during the second wave of COVID-19, a fact rediscovered in our analysis wherein 45.5% of HICPs were advised blood thinners to reduce hospitalisation and/or thrombosis[19,20]. Intriguingly, the most commonly advised blood thinner (government and private doctors) was ecosprin. This perhaps substantiates the early use of aspirin in COVID-19 patients, which has documented effects of inhibiting virus replication, anti-platelet aggregation, anti-inflammatory, and anti-injury activity, reducing the incidence of severe and critical patients, shortening hospital stay and decreasing cardiovascular complications[21].

Among the various available drugs, vitamin C and Zinc were ubiquitously advised as a part of supportive treatment protocol by 90% of the doctors. The water-soluble ascorbic acid has reported antioxidant properties and acts as a free radical scavenger. It is anti-inflammatory and influences cellular immunity and vascular integrity. It also serves as a cofactor in endogenous catecholamine generation, and hence, it beneficially affects influenza and many diseases, thus making it a preferred drug candidate to be included in the management protocol for COVID-19[22]. A word of caution is the opinion stated by the NIH guidelines "There is insufficient evidence for the panel to recommend either for or against the use of vitamin C for the treatment of COVID-19 in non-hospitalised patients". This stems from their rationality that patients who are home-isolated are not experiencing any oxidative stress or severe inflammation that warrants the prescription of vitamin C in HICPs, and, therefore, the use of vitamin C still needs to be elucidated. On a similar rationale, even though zinc competently spoils RNA virus's replication, there is insufficient evidence in favour of zinc for the treatment of HICPs[23]. In addition, doctors recommended vitamin D3 to HICP as vitamin D3 levels have been reported to be low in COVID-19 patients, and they play an important role as immunomodulatory and anti-inflammatory[24]. The use of ivermectin and steroids as a treatment modality in the Indian context by 60% of the doctors is thought-provoking as ivermectin was given preferably to hospitalised patients, and steroids were not mentioned in WHO guidelines. Ivermectin is an FDA-approved anti-parasitic drug that has been used in the treatment of more than 30 diseases. However, during the unprecedented COVID, it was not under the recommended regime from WHO but was used as an additional drug by doctors in India as it was shown to have significant effects on the reduction of viral loads[25].

Furthermore, a high frequency of oral steroids, especially dexamethasone, was prescribed by private doctors in comparison to government doctors who preferred to recommend antibiotics over steroids to HICP. Among the various available antibiotics, doctors preferred azithromycin, which is an antibiotic with proven beneficial effects due to its immunomodulatory properties, maintaining epithelial integrity, and preventing lung fibrosis in viral infections. It was given as a regime along with other steroids to patients as it has been shown to reduce mortality and ventilation days[26]. However, further clinical trials showed no additional benefit to HICPs, though it was continued as a supportive antibiotic in hospitalised patients and later on was not recommended in COVID-19 patients.

Similarly, another antibiotic prescribed by doctors to HICPs was doxycycline, which is known for its antiviral and anti-inflammatory effects, thereby preventing lung damage. However, other studies showed no proven benefits to HICP, and now doxycycline is no longer recommended[27]. Further, oral corticosteroid was not recommended by the WHO in the treatment of COVID-19[28]. There is a paucity of data that supports the use, efficacy and safety of systemic corticosteroids in non-hospitalised patients with COVID-19. On the contrary, it is coupled with adverse events like hyperglycemia, neuropsychiatric symptoms and secondary infections, which in HICP, at times, become difficult to detect and monitor. Among the different available steroids, the most recommended steroids were methylprednisolone>prednisolone >dexamethasone> hydrocortisone. However, clinical trials have shown

the role of methylprednisolone in the treatment of severe or hospitalised COVID-19 patients[29]. The studies demonstrating the use of methylprednisolone in HICPs are limiting. However, its use in the treatment of severe COVID-19 patients results in statistically significant faster recovery than the use of dexamethasone, which is well documented[30].

This study showed a high frequency of fabiflu drugs were advised to HICPs by private doctors in comparison to government doctors. Although fabiflu was not recommended by WHO, a few studies showed the *in vitro* activity of fabiflu in rapid clearance of SARS-CoV-2[31]. Therefore, some states in India included fabiflu for the treatment of COVID-19 patients. Apart from fabiflu, an antiviral drug hydroxychloroquine (HCQS) was also advised, which is known to have low efficacy, but ICMR guidelines allowed its use in the management of COVID-19 patients to combat the pandemic. A recent study also showed that HCQS was well tolerated by COVID-19 patients and had no cardiac-related adverse effects[32].

Conclusion

Overall, doctors from both types of hospitals followed the WHO-recommended guidelines in the treatment of HICPs. Since clinical trials were missing and the penchant was to reduce mortality and morbidity while successfully reassuring the health of the common man who was home-isolated, any recommendation from any valid medical institution or government guidelines seemed to be strictly followed. However, differences in steroids, drugs and CT scan recommendation, perhaps a stretched comment, can be inferred in treatment modality by private and government hospitals due to differences in accessibility and affordability of the HICP to approach the health care facilities and, of course, the commercial opportunity available to doctors.

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