Original Article

Infection Pattern, Treatment Protocols and Post-COVID-19 Complications–A Survey on 706 COVID-19 Recovered Participants

Ravindra Semwal[1], Ankit Kumar[1], Ashutosh Chauhan[2], Ruchi Badoni Semwal[3] , Navin Chandra Joshi[4], Sunil Kumar Joshi[5] and Deepak Kumar Semwal[6]*

[1]*Research and Development Centre, Faculty of Biomedical Sciences, Uttarakhand Ayurved University, Harrawala, Dehradun, Uttarakhand, India;* [2]*Department of Biotechnology, Faculty of Biomedical Sciences, Uttarakhand Ayurved University, Harrawala, Dehradun, Uttarakhand, India;* [3]*Department of Chemistry, VSKC Government Postgraduate College, Dakpathar, Uttarakhand, India;* [4]*Department of Swasthvritta and Yoga, Faculty of Ayurveda, Uttarakhand Ayurved University, Harrawala, Dehradun, Uttarakhand, India;* [5]*Uttarakhand Ayurved University, Harrawala, Dehradun, Uttarakhand, India;* [6]*Department of Phytochemistry, Faculty of Biomedical Sciences, Uttarakhand Ayurved University, Harrawala, Dehradun, Uttarakhand, India*

Abstract

Background and objectives: The pandemic of coronavirus disease 2019 (COVID-19) has killed millions of people globally and has severely affected quality of life and global economy. The present randomized survey aimed to collect information based on vaccination, symptoms, treatments, and post-COVID-19 complications from participants that recovered from COVID-19 to find out the disease pattern, trends, and effective treatment protocols.

Methods: The information from participants was collected by an online questionnaire that was circulated among the population of India through emails and social media.

Results: A total of 706 responses were recorded from participants that recovered from COVID-19 from 20 Indian states. Males and females from all age groups took part in the online survey. Among them, 77% of the participants were not vaccinated and 17% were vaccinated with a single dose and 6% with a booster dose. An average of 27% of the total vaccinated participants had a comorbidity that included diabetes, hypertension, and pulmonary disease. Most of the patients with moderate to severe symptoms preferred allopathic treatment. The adoption level of allopathic treatment was significantly higher ($p = 0.001$) than other treatment options. The results showed that 12% of the patients adopted the Ayurvedic treatment and 14% preferred a mixed treatment. Approximately one-third of the participants had various post-COVID-19 complications that were related to breathing and anxiety.

Conclusions: The survey concluded that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected almost the whole population irrespective of gender, age, and region. The study further concluded that vaccination is the main protection against SARS-CoV-2 infection.

Introduction

Coronavirus disease 2019 (COVID-19) emerged as a global pandemic in 2020 that caused millions of deaths worldwide.[1] COV-

ID-19 is the first pandemic that spread to 220 countries and affected almost the whole population, irrespective of region and race. The epicenters of COVID-19 have changed with time. After the first report of COVID-19 in China, the first epicenter was in Italy and thereafter it spread to the US, Brazil, India, Germany, South Africa, Russia, France, the UK, Turkey, Argentina, Spain, Mexico, and many other countries within a very short time.

COVID-19 is categorized under communicable diseases, as it transmits from person to person, through respiratory droplets, aerosols, and direct contact. In early studies, the incubation period of coronavirus was reported to be 5.2–6.4 days, but some reports also suggested 19 days, although this longer incubation period is considered as a low probability event.[2] Currently, various diagnostic tests are used for the confirmation of COVID-19 that include real-time reverse transcription-polymerase chain reaction (RT-PCR) and rapid antigen tests (RAT).[3]

RAT is a ready-made kit that is widely accepted for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for mass sampling. It detects the presence of viral proteins by a lateral flow assay. This test targets the N-protein, which is the most abundantly expressed by SARS-CoV-2. However, a RAT only assesses acute infection and chronic infection or the bodies' response to vaccination is not detected.

To date, many variants of coronavirus have been identified in which Alpha (B.1.1.7), Beta (B.1.351, B.1.351.2 and B.1.351.3), Gamma (P.1, P.1.1, P.1.2, P.1.4, P.1.6 and P.1.7), and Delta (B.1.617.2, AY.1, AY.2, AY.3 and AY.3.1) are of high concern.[4] Among them, the B.1.617.2 strain of Delta variant is lethal and is 40–60% more transmissible than the Alpha variant and almost twice that of the original Wuhan strain.[5] Of interest, most of the existing vaccines are effective against all variants including Delta.[6] In addition, the most recently identified variant Omicron is a high concern and spreading faster than the earlier variants. However, the research outcomes that are based on this variant are premature and no conclusions can be drawn at this stage.

SARS-CoV-2 has different protein structures with a non-segmented enveloped and positive-sense single-stranded RNA.[7] Linear and helical capsids are found on the surface of the virus and the nucleocapsid remains is in the envelope of the virion.[8] The spike protein plays an important role in the recognition of the receptor and fusion of the cell membrane. This protein has two subunits called S1 and S2 in which the S1 subunit has a receptor-binding domain to bind the host receptor ACE2; therefore, SARS-CoV-2 can enter the host cell using ACE2 as the receptor. However, the S2 subunit is the mediator during fusion of the cell membrane through a six-helical bundle formation.[9]

India was one of the countries most affected by COVID-19, particularly during the second wave. Once, from April to May 2021, there was a stage came when patients could not get treatment because the beds were occupied beds in all the hospitals dedicated to COVID-19 patients across the country.[10] COVID-19 affects a patient during the infection and after recovery with post-COVID-19 complications. The present study was designed to collect information based on symptoms, treatments, and post-COVID-19 complications from patients that recovered from COVID-19 in India to understand the pattern of infection and effectiveness of the treatments received; therefore, a new treatment protocol or prophylaxis could be suggested.

Materials and methods

A bilingual online questionnaire in Hindi and English was pre-

pared that used Google Forms to collect information from patients that recovered from COVID-19 in India. The questionnaire was circulated through email, WhatsApp, and Facebook with the title "Scientific Analysis of COVID-19 Recovered Cases by Uttarakhand Ayurved University (Govt. of Uttarakhand)". The form was composed of eleven questions, such as the method for the diagnosis of COVID-19, when they tested positive, comorbidity, the severity of overall symptoms, when symptoms appeared, standard operating procedure followed, treatment protocol, treatment during hospitalization (if hospitalized), time taken for recovery, post-COVID-19 complications, and treatment choice for post-COVID complications. Most of the questions had >2 options in which a participant could select >1 option. A declaration that stated "the personal data of the participant will be kept confidential and not published without prior consent" was included in the questionnaire (Supplementary File 1).

This study was conducted between 1 May 2021 and 31 October 2021 with support from the state government and local administrations. The Minister of Ayurveda, Yoga and naturopathy, Unani, Siddha and Homeopathy (AYUSH) and AYUSH Education (Government of Uttarakhand) officially released the questionnaire and it was widely circulated among the population through different social media platforms. In addition to circulating it through the social media accounts of the authors, the questionnaire was sent to approximately 1,500 contacts individually by their WhatsApp numbers and email IDs irrespective of their state. The contacts were accessed from the saved mailing lists of the authors' emails and WhatsApp numbers that were saved in the contact list of each author. The responses with incomplete information were excluded from the present study. Finally, the data were analyzed by intercorrelating the information.

The protocol for the collection, analysis, and publication of data was approved by the Institutional Ethics Committee of Uttarakhand Ayurved University, Dehradun, India (Ref. No. 2012). The committee suggested not to disclose or publish any personal information of any patient that took part in the present survey and therefore, the data based on personal information remained confidential.

Statistical analysis

The collected data was analyzed to determine the statistical significance of the results. A chi-square test was applied to calculate *p*-values using SPSS 16.0 software. The results with $p<0.005$ were considered statistically significant.

Results

Geographical distribution of participants

A total of 706 participants (418 male and 288 female) from 20 states in India participated in the survey, which was limited to people that had recovered from COVID-19. The highest number of participants were recorded in Uttarakhand State (463) followed by Delhi (66), Uttar Pradesh (47), and Haryana (32). The state-wise distribution of participants is given in Figure 1.

Age and occupation based distribution of participants

Of interest, participants from almost all age groups participated in the present survey. Most of the participants were aged 16–30
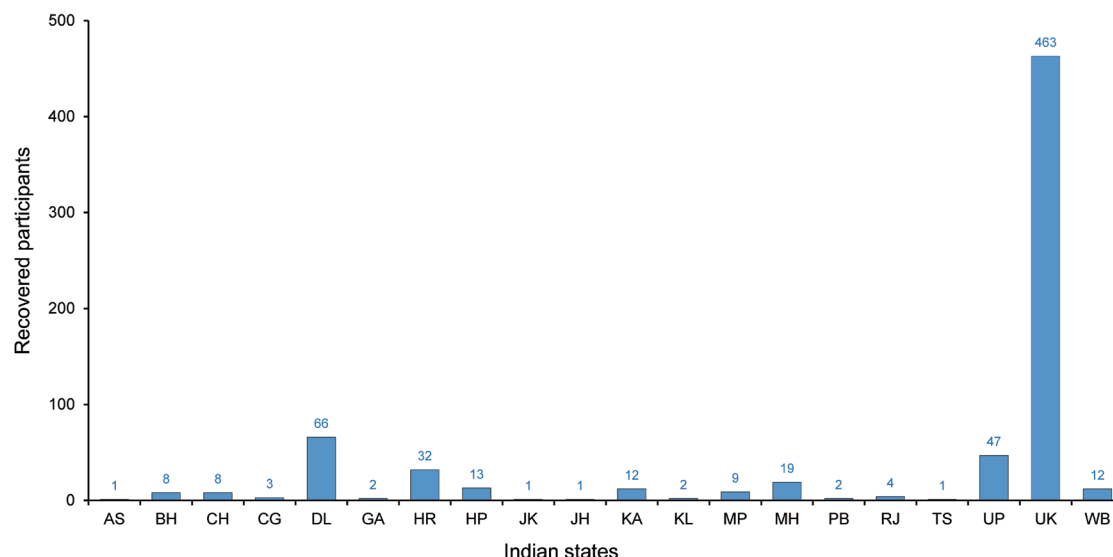
Fig. 1. Distribution of COVID-19 recovered participants from different Indian states. AS: Assam, BH: Bihar, CH: Chandigarh, CG: Chhattisgarh, DL: Delhi, GA: Goa, HR: Haryana, HP: Himachal Pradesh, JK: Jammu and Kashmir, JH: Jharkhand, KA: Karnataka, KL: Kerala, MP: Madhya Pradesh, MH: Maharashtra, PB: Punjab, RJ: Rajasthan, TS: Telangana, UP: Uttar Pradesh, UK: Uttarakhand, WB: West Bengal.

years (305) followed by 31–45 years (182), 46–60 years (118), ≤15 years (55), and >60 years (46). The data further revealed that 310 participants were working, 232 were students, and 103 were either homemakers or non-working, and 61 participants did not disclose their occupation.

Method of diagnosis

The present study included confirmed cases of COVID-19 that used any of the valid diagnostic methods. RT-PCR was most accurate in the diagnosis of COVID-19. Among the participants, 464 participants underwent RT-PCR tests and 185 were diagnosed with coronavirus infection by RAT. After recovery, 43 participants used an antibody test to confirm COVID-19 in the recent past. In addition, six participants stated that the doctor confirmed their infection with the help of a chest computed tomography scan or X-rays. However, eight participants did not mention any diagnosis method, they started treatment after being in contact with a positive patient and feeling COVID-19 like symptoms.

Vaccination status

Of note, 544 (77.05%) participants were non-vaccinated, where most of the participants were aged 15–30 years, for instance, mostly students. The reason behind the non-vaccination of younger age groups is the systematic drive for vaccination in India, which started with frontline health workers followed by senior citizens (i.e., >60 years), citizens aged 45–60 years, and a younger population between aged 18 and 45 years. A total of 121 participants had received the first dose of vaccine and 41 participants had been vaccinated with a booster dose.

Comorbidity status

Earlier research proved that patients with diabetes, cancer, hyper-

tension, or lung diseases were more prone to COVID-19. Therefore, data based on comorbidity were collected to correlate the results with positive cases. The results showed that most of the participants, for instance, 64 were diabetic patients and 32 were living with hypertension. The distribution of participants according to the comorbidity reports is shown in Figure 2.

Symptoms and severity

A total of 111 participants confirmed that they had no symptoms during coronavirus infection. Most of the cases (298) were in the moderate symptomatic category, followed by mild (188), and severe (109). Among all the symptomatic participants, common symptoms, such as fever, fatigue, body aches, and headache appeared in 445 cases in which 144 participants disclosed symptoms, such as a runny nose or nose congestion, sneezing, dry cough, and
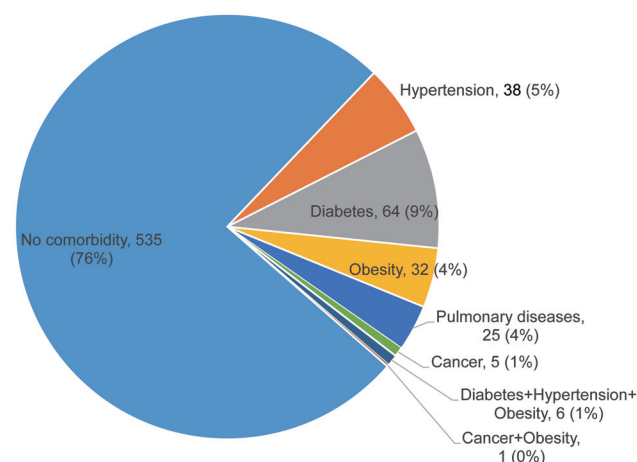

Fig. 2. Status of comorbidity in participants that recovered from COVID-19 in the present survey.
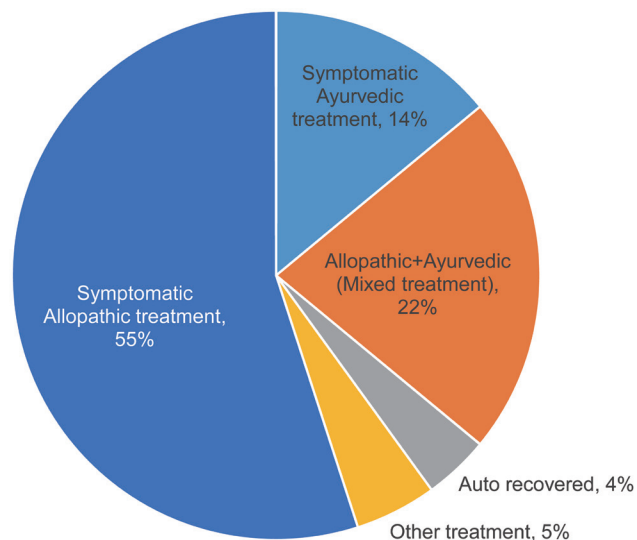
Fig. 3. Different treatment options adopted by participants during COVID-19 and their preference percentage.

sore throat. Difficulty in breathing or shortness of breath, chest pain and toughness were recorded in 60 cases and loss of taste, smell, or both were disclosed by 111 participants. Diarrhea, stomachache, and abdominal cramps were reported in 50 cases and loss of speech, movement, or both were found in 21 cases. Moreover, 22 participants declared conjunctivitis, redness of the eyes, or both, and 13 participants mentioned all the above symptoms during their hospitalization.

Treatment preference

According to local government guidelines on isolation and hospitalization for COVID-19 patients, 481 cases were either advised to home isolate or the participants themselves chose to isolate at home. With increasing severity, 84 patients were admitted to general COVID-19 isolation centers and 92 participants with high severity were admitted to higher COVID-19 hospitals. However, 49 participants stated that they isolated at government authorized hotels or hostels during the infection. Overall, 388 patients received symptomatic allopathic treatment prescribed by clinicians that included paracetamol, azithromycin, doxycycline, ivermectin, cetirizine, zinc, vitamin C, vitamin D3, and multivitamins on a case-to-case basis. In addition, Indian traditional medicine-based treatments were followed by 96 participants who received symptomatic AYUSH treatments prescribed by AYUSH practitioners that included gargling and steam inhalation with selected Ayurvedic herbs, AYUSH Kadha, Aswagandha, Guduchi, Peepali, AYUSH 64, Coronil and Chyawanprash with regular yoga and meditation. Of interest, 158 patients received a mixed treatment of Ayurveda and Allopath. In total, 32 participants recovered without taking any medication and 32 participants mentioned other treatments (Fig. 3).

Treatment status of hospitalized patients

The data confirmed that 176 patients were admitted to COVID-19 hospitals from which 137 patients were discharged after general care with oxygen support and symptomatic allopathic treatment. In total, 34 patients underwent intensive care with oxygen support

and a specific COVID-19 treatment that included remdesivir and steroidal therapy. Moreover, only five patients underwent intensive care with ventilator support and remdesivir and plasma therapy.

Recovery duration

Analysis of the data revealed that 158 patients recovered in <7 days, which included asymptomatic cases. Approximately 50% (351) participants reported that they recovered in 7–14 days and 148 cases recovered in 15–21 days. However, out of 109 severe patients, 49 recovered after ≥21 days.

Post-COVID-19 complications and treatment

General complications, such as tiredness, dizziness, joint or muscular pain, and weight loss were recorded in 211 participants, in which 49 cases complained of difficulty in thinking or concentrating, depression or anxiety, and headache. A total of 35 participants complained of heart palpitations, chest pain, breathing difficulty, and cough and 62 cases lost either smell, taste, or both. Moreover, seven patients stated that they had all of the previous symptoms after recovering from COVID-19. Most of the participants with post-COVID-19 complications preferred complete bed rest without taking any medication, and 107 patients received symptomatic allopathic treatment, such as painkillers, bronchodilators, and nootropic supplements together with vitamins and health tonics and 63 received symptomatic Ayurvedic treatment, such as Chyawanpras Rasayana, Shwaskuthar ras, and Peedantak vati together with yoga and meditation.

Data correlation with vaccination

The survey showed that 543 (77%) of participants were non-vaccinated, 121 (17%) were vaccinated with a single dose, and 42 (6%) were vaccinated with a booster dose. Currently, two vaccines (Covishield from Serum Institute of India Pvt. Ltd., Pune, Maharashtra, India and Covaxin from Bharat Biotech, Hyderabad, Telagana, India) are commonly used in India and other vaccines, such as Sputnik V (Gamaleya National Center of Epidemiology and Microbiology, Moscow, Russia) and mRNA-1272 (Moderna, Cambridge, MA) have been approved; however, they have only been used in very small population. Covaxin is an inactivated vaccine and was developed using whole virion inactivated Vero cell derived platform technology. Covishield is a non-replicating viral vector vaccine. This recombinant vaccine is produced using a replication-deficient chimpanzee adenovirus vector, which encodes the SARS-CoV-2 Spike (S) glycoprotein. It is produced in genetically modified human embryonic kidney (HEK) 293 cells. For efficacy, a randomized phase III controlled trial was carried out between November 2020 and January 2021 on 24,419 participants, which revealed that the BBV152 vaccine (Covaxin) was highly effective against symptomatic COVID-19 adult patients. In India, its overall efficacy was 77·8% with no safety concerns.[11] However, a cohort study that was carried out on 1,595,630 cases from the Indian armed forces and frontline medical workers revealed that the AZD1222 vaccine (Covishield) was 91.8–94.9% effective against COVID-19.[12]

According to the Ministry of Health and Family Welfare (Government of India), on 21 November 2021, 1,16,50,55,210 vaccine doses have been given across the country, which included 76,44,55,428 first doses and 40,05,99,782 second doses. Of inter-
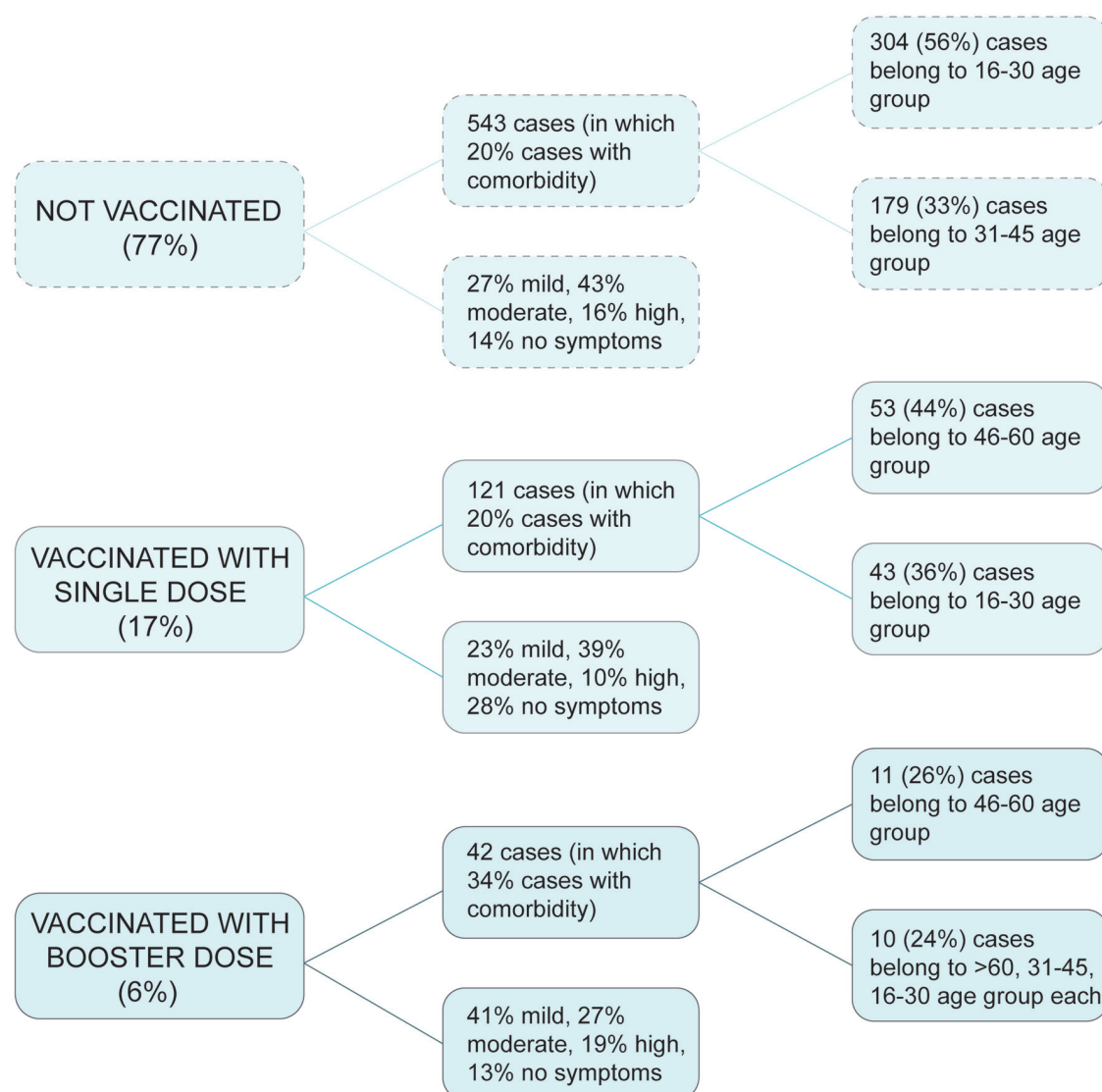
Fig. 4. Random correlation of data based on vaccination, symptoms, comorbidities, and age of participants.

est, the Covishield vaccine accounts for >80% of the total vaccine doses that have been administered in India.

The present data showed that vaccines have a major role in protecting from coronavirus infection. Moreover, a booster dose was highly effective against SARS-CoV-2. In addition, the data showed that vaccinated participants possessed mild to moderate symptoms and were rarely hospitalized. Of note, hospitalized patients had comorbidities, such as diabetes and hypertension. A random correlation of the data with vaccination is shown in Figure 4.

Statistical interpretation of data

As given in Table 1, the number of symptomatic cases without vaccination was significantly ($p=0.002$) higher than that of single vaccinated cases those with a booster dose. The data revealed a sharp decrease in symptomatic patients with vaccination, in which the booster dose was much better than a single dose at reducing the symptoms. Similarly, a significant ($p=0.003$) difference was found

between vaccinated and non-vaccinated cases with comorbidities. In this case, the results of booster doses were highly significant.

Considering the treatment options and the severity of symptoms, the results revealed that the adoption level of allopathic treatment was significantly higher ($p=0.001$) even in mild cases followed by high ($p=0.002$) and moderate ($p=0.003$) symptomatic cases. Overall, the allopathic treatment performed four times bet-

Table 1. Statistical significance of vaccination status with symptoms and comorbidities

Vaccination status	Cases with symptoms	Cases with comorbidities
Not vaccinated	467 (57.64%)	109 (15.43%)
Vaccinated with single dose	87 (12.32%)	24 (3.39%)
Vaccinated with booster dose	36 (5.09%)	14 (1.98%)
p-value	0.002	0.003

Table 2. Statistical significance of treatment options with the severity of symptoms

Treatment option	Cases with mild symptoms	Cases with moderate symptoms	Cases with high symptoms
Allopath	105 (14.87%)	165 (23.37%)	69 (9.77%)
AYUSH	18 (2.54%)	51 (7.22%)	13 (1.84%)
Mixed treatment	43 (6.09%)	47 (6.65%)	11 (1.55%)
p-value	0.001	0.003	0.002

AYUSH, Ayurveda, Yoga and naturopathy, Unani, Siddha, and Homeopathy.

ter than the AYUSH treatment. However, the cases that adopted a mixed treatment were higher than the AYUSH treatment, particularly in mild symptomatic cases (Table 2).

Moreover, the multiple regression analysis indicated that mild, moderate, and severe cases of COVID-19 had high, moderate, and low recovery times, respectively. The comorbidities and age of patients predicted worse clinical outcomes for severe COVID-19 infection.

Discussion

Although millions of people were infected with SARS-CoV-2 in India during the first and second waves,[13] very few people participated in the present survey, which was probably due to a reluctance to disclose their identity and data to the surveyor. In the present study, >65% of participants were recorded from Uttarakhand State in which most of the participants were contacted personally and convinced to participate. Some other states, such as Delhi, Haryana, and Uttar Pradesh recorded a suitable number of participants. Overall, adequate diversity in the participants was gathered from different parts of India.

Diagnosis of COVID-19 by RT-PCR test was considered to be the most acceptable method, because in certain cases, the patients that had a negative report from RAT were positive with an RT-PCR test. In the present survey, approximately 66% of the participants underwent RT-PCR test and 26% of cases were confirmed by RAT. The most common symptoms recorded during COVID-19 in mild cases were fever and upper respiratory tract infections without shortness of breath or hypoxia. These patients were advised to take rest at home and isolate and were prescribed symptomatic treatment with 3 mg ivermectin/day for 3 days and 400 mg hydroxychloroquine (HCQ)/week for 4 weeks with 650 mg paracetamol (only with fever and body aches). Moreover, budesonide inhalation was prescribed for patients with increasing symptoms that were related to respiration after 5 days of disease onset.

However, patients who had a respiratory rate >24/m, breathlessness, and oxygen saturation (SpO$_2$) between 90% and 93% were considered as moderate cases. These patients received oxygen support with anti-inflammatory or immunomodulatory therapies, such as methylprednisolone or dexamethasone injections. In addition, anticoagulating drugs, such as heparin or enoxaparin were prescribed. However, patients with a respiratory rate >30/m, breathlessness, and SpO2 <90% were considered as severe cases. These patients received respiratory support and were admitted to the intensive care unit (ICU). Methylprednisolone or dexamethasone injections together with heparin or enoxaparin were commonly given to these patients. Under specific circumstances, remdesivir and tocilizumab were given to these patients.[14] In addition, some clinicians frequently prescribed favipiravir instead of remdesivir. In addition, vitamin C and zinc were commonly prescribed to all positive cases. A combination of HCQ (400 mg twice for the first day followed by 200 mg twice for 4 days) and azithromycin (500 mg/day for 5 days) was prescribed to some patients with severe conditions under appropriate medical supervision.[15] However, at a later stage, the Indian Council of Medical Research task force strongly discouraged the use of HCQ for the general public without medical supervision.[16] Thereafter, the union health ministry withdrew many popular drugs, such as ivermectin, azithromycin, doxycycline, zinc, favipiravir, and plasma therapy from the COVID-19 protocol due to their insignificant results.[17] The present survey showed that 55% of patients, of which most were severe cases, received allopathic treatment and 22% of patients received mixed treatments.

In addition, the Ministry of AYUSH, Government of India[18] issued guidelines based on Ayurveda and Yoga for the management of COVID-19. According to the protocol, a 500 mg extract of Ashwagandha (*Withania somnifera*), 500 mg extract of Guduchi (*Tinospora cordifolia*), or 10 g of Chyawanprash with warm water or milk were recommended for prophylactic care. For asymptomatic COVID-19 patients, a 500 mg extract of Guduchi (*T. cordifolia*) or a 375 mg extract of a combination of Guduchi (*T. cordifolia*) and Pippali (*Piper longum*), or 500 mg of AYUSH-64 (a polyherbal formulation composed of 100 mg of a bark extract from Saptaparna (*Alstonia scholaris*), 100 mg root extract of Katuki (*Picrorhiza kurroa*), 100 mg extract of the whole plant of Kiratatikta (*Swertia chirata*) and 200 mg of seed powder of Kuberaksha (*Caesalpinia crista*) in each 500 mg tablet). COVID-19 patients with mild symptoms, such as fever, headache, tiredness, dry cough, sore throat, and nasal congestion were recommended to take a 375mg extract of a combination of Guduchi and Pippali and 500 mg of AYUSH-64. In addition to these medicines, general and dietary measures were suggested to be followed, which included some yoga postures and food regimes. However, the Ministry did not issue any guidelines for patients with moderate or severe symptoms. This protocol contains guidelines for patients with post-COVID-19 complications, such as lung complications (i.e., fibrosis), fatigue, and mental problems. For these patients, a 500 mg extract of Ashwagandha, 10 g Chyawanprash, and 3 g Rasayana Churn, a mixture of equal amounts of Guduchi, Amlaki (*Emblica officinalis*), and Gokharu (*Tribulus terrestris*)/ for 15 days was recommended. In the present survey, 14% of patients received AYUSH treatment and 22% of patients received mixed treatment. Overall, 36% of patients had faith in their AYUSH treatment during COVID-19.

Earlier reports suggested that a large number of patients complained of different complications after recovering from COVID-19.[19,20] These complications were acute, such as breathing difficulty, stress, fatigue, vomiting, joint pain, and weight loss. Almost one-third of the participants recorded mild to moderate post-COVID-19 complications. Moreover, very few participants (5%) had severe complications, such as heart palpitations, chest pain, breathing difficulties, and a cough. Out of the participants with post-COVID-19 complications, approximately 50% received symptomatic allopathic treatment and 30% of patients preferred an Ayurvedic treatment that included yoga and meditation.

Limitations of the study

The present study has some limitations. The majority of participants were younger (18–45 years) without comorbidities; therefore, the results cannot be generalized. Another limitation of the study was the selection of the participants. The present data were obtained from survivors who could respond, and patients with severe diseases or death were not included in this study, because they could not respond to the questionnaires. Moreover, this research was a survey, and therefore, could not comment on treatment efficacy. Therefore, future prospective studies should be carried out to test the efficacy of treatment options.

Future directions

The results of the present study indicated that vaccination is effective in protecting from COVID-19 and reducing the severity of symptoms. Therefore, the vaccination drive must increase on a global level irrespective of the country's development status. Although allopathic treatment was effective when treating symptomatic patients and covered the majority of the population, Indian traditional medicine (AYUSH) played an important role either in protecting from infection or treating COVID-19 patients. Therefore, traditional medicines should be promoted as treatment options, mainly for mild to moderate COVID-19 patients.

Conclusions

The present study concluded that vaccination plays a key role in combating coronavirus. It is effective at protecting from COVID-19 infection and effective at reducing the severity of symptoms. The most important part of the present survey was the treatment choice of the COVID-19 patients. The majority of the patients underwent allopathic treatment and approximately one-third of participants trusted Ayurvedic or mixed treatment, particularly those with mild to moderate symptoms. Moreover, post-COVID-19 complications were noted in hospitalized patients with severe symptoms. The treatment choice for post-COVID-19 complications had a similar ratio as that recorded for the treatment of COVID-19.

Supporting information

Supplementary material for this article is available at https://doi.org/10.14218/ERHM.2021.00069.

Supplemental File 1. The questionnaire.

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Conflict of interest

The authors have no conflicts of interest related to this publication.

Author contributions

RS: data collection and manuscript writing; AK: material support and data collection; AC: interpretation of data and statistical analysis; RBS: data collection and manuscript writing; NCJ: data collection and technical support; SKJ: administration and critical revision; DKS: study design, interpretation of data, critical revision and editing. All authors have made a significant contribution to this study and have approved the final manuscript.

Ethical statement

The protocol for the collection, analysis, and publication of data was approved by the Institutional Ethics Committee of Uttarakhand Ayurved University, Dehradun, India (Ref. No. 2012). The committee suggested not to disclose or publish any personal information of any patient that took part in the present survey and therefore, the data based on personal information remained confidential.

Data sharing statement

No additional data are available.

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