Homeopathic Medicines in Second Wave of COVID-19: Prognostic Factor Research

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Abstract

Background The clinical profile and course of COVID-19 evolved perilously in a second wave, leading to the use of various treatment modalities that included homeopathy. This prognostic factor research (PFR) study aimed to identify clinically useful homeopathic medicines in this second wave.

Methods   This was a retrospective, multi-centred observational study performed from March 2021 to May 2021 on confirmed COVID-19 cases who were either in home isolation or at COVID Care Centres in Delhi, India. The data were collected from integrated COVID Care Centres where homeopathic medicines were prescribed along with conventional treatment. Only those cases that met a set of selection criteria were considered for analysis. The likelihood ratio (LR) was calculated for the frequently occurring symptoms of the prescribed medicines. An LR of 1.3 or greater was considered meaningful.

Results   Out of 769 confirmed COVID-19 cases reported, 514 cases were selected for analysis, including 467 in home isolation. The most common complaints were cough, fever, myalgia, sore throat, loss of taste and/or smell, and anxiety. Most cases improved and there was no adverse reaction. Certain new symptoms, e.g., headache, dryness of mouth and conjunctivitis, were also seen. Thirty-nine medicines were prescribed, the most frequent being *Bryonia alba* followed by *Arsenicum album*, *Pulsatilla nigricans*, *Belladonna*, *Gelsemium sempervirens*, *Hepar sulphuris*, *Phosphorus*, *Rhus toxicodendron* and *Mercurius solubilis*. By calculating LR, the prescribing indications of these nine medicines were ascertained.

Conclusion   Add-on use of homeopathic medicines has shown encouraging results in the second wave of COVID-19 in integrated care facilities. Further COVID-related research is required to be undertaken on the most commonly prescribed medicines.

Keywords

► COVID-19
► second wave
► homeopathy
► prognostic factor research
► likelihood ratio

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first appeared in late 2019 in Wuhan Province, China.[1] It was declared a pandemic by the World Health Organization (WHO). In April 2020 India had faced the first wave, which started receding by December 2020. However, in March 2021 India was hit by the second wave of coronavirus. On September 30, 2021, the COVID-19 cases had reached a total of 33.76 million, with more than 448,000 deaths.[2] The second wave had evolved at a faster rate as compared with the first wave.[3]

There could be several factors responsible for the increased number of cases in the second wave that allowed substantial numbers of viral replication, mutation, and evolution.[4] The SARS-CoV-2 virus had mutated and this coronavirus variant, known as SARS-CoV-2 B.1.617, had been declared as a "variant of global concern" by the WHO.[5] Lineage B.1.617.2 had been designated as variant Delta, believed to spread faster than other variants.[6,7] It was highly infectious and more pathogenic than the initial strains.[8] It had more effective transmission capability and its incubation period was also less.[3] It was less affected by contemporary vaccination, and was the central cause of the COVID-19 second wave in India.[6,8] Certain studies reported the presence of a triple-mutant strain, B.1.618, as strongly associated with India's deteriorating COVID-19 situation.[9]

Some parts of the country, e.g., Maharashtra, Tamil Nadu, Delhi, Gujarat, Telangana, Karnataka and Uttar Pradesh, were especially badly affected.[10] People were struggling to come to terms with the magnitude of the wave, as there was an acute shortage of hospital beds, oxygen supply, essential medicines and ventilators for COVID-19 patients and, most unfortunately, many families were losing their dear ones to the disease. In addition, several cases with positive COVID-19 symptoms were negative on the RT-PCR test.[3,10]

Apart from the common symptoms of fever or chills, cough, tiredness, myalgia, sore throat, and a loss of sense of taste or smell, there were some newer signs of COVID-19 infection in the second wave: e.g., sudden loss of or diminished hearing, tinnitus, conjunctivitis, skin rashes, dry mouth, and headache lasting for a long time.[11]

Especially gastrointestinal symptoms were also variable: e.g., loss of appetite, vomiting, stomach pain and diarrhea.[12,13] Extreme lethargy was reported as one of the early symptoms of the COVID-19 infection during the second wave.[11,14] Cases of dyspnea were more common, sometimes being the first sign of infection, and with a drop in oxygen saturation (SpO_2 levels).[3,11] The pediatric and younger individuals were also getting infected more frequently.[15]

In the second wave, the health system was overwhelmed by the new strain's highly infectious nature and changing symptomatology. Conventional treatment was mainly symptomatic—hydration, anti-pyretics, anti-tussive, multi-vitamins, anti-inflammatory or immunomodulatory therapy, steroids, anti-coagulants and oxygen support, or therapies based on limited available evidence, e.g., ivermectin, hydroxychloroquine, remdesivir and tocilizumab.[16,17] Patients were

also seeking AYUSH (Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy) treatments along with conventional treatment.

Homeopathic medicines are prescribed based on symptoms, regardless of the nosological diagnosis. The prescriptions are based on the symptoms of the patient: i.e., prognostic factors, which are the characteristics of a patient that can be used to estimate the chance of recovery from a disease. In epidemics, most of the patients suffer from similar complaints/symptoms. These seemingly common symptoms assume importance if prognostic factor research (PFR) is done, guiding the clinician toward accurate medicine selection.[18]

Studies had found homeopathic medicines to be useful during the first wave of COVID-19.[19–21] Some homeopathic medicines, e.g., *Arsenicum album, Bryonia alba, Gelsemium sempervirens, Pulsatilla nigricans* and *Mercurius solubilis*, were identified. During the first wave also, bias was noticed in some data collections.[22,23] All the doctors working in the Delhi Government were trained in data collection when the first wave started and also afterward, before the onset of the second wave, to upgrade their data collection skills. During the second wave, symptoms were capricious and of increased intensity, and patients were overwhelmed due to the disease and sought homeopathic consultations at Integrated Delhi Government Health Centres (IDGHCs), wherein conventional as well as homeopathic services are provided under one roof.

Objectives

The primary objective was to identify clinically useful homeopathic medicines in the COVID-19 second wave and their characteristic indications by using PFR to calculate the likelihood ratio (LR) of symptoms with respect to the most frequently used medicines.

The secondary objective was to compute the symptomatology of the second wave of COVID-19.

Methods

Study Design and Settings

This was a retrospective, open label, multi-centred observational study performed from March 2021 to May 2021 on confirmed COVID-19 cases. A confirmed COVID case was defined as: a person with a positive Nucleic Acid Amplification Test, including real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay, of nasal and pharyngeal swab specimens; a patient who has tested positive in SARS-CoV-2 Antigen-RDT (rapid diagnostic test) and meeting either the probable case definition or the suspect criteria *or* an asymptomatic person with a positive SARS-CoV-2 Antigen-RDT who was a contact with a probable or confirmed case.[17]

The study was performed at IDGHCs and at COVID Care Centres (CCCs). Patients who visited these centers were treated with homeopathic medicines along with the standard conventional treatment advocated. Under proper

COVID-19 protection precautions, a first in-person consultation was provided after recording all necessary details such as the patient's credentials, symptoms, temperature and SpO2. Homeopathic medicines were prescribed based on the individualized symptoms of each patient. Homeopathic doctors were free to prescribe any medicine that they felt was best suited in a case, as per their clinical acumen. In total, 41 qualified homeopathic doctors with experience of 3 to 25 years submitted data recorded in a specially designed format. A single medicine was prescribed to most of the individual patients; a few patients were prescribed two or more medicines. Patients were advised home isolation and were provided with a pulse oximeter and a thermometer for self-monitoring. These patients were followed up telephonically on a daily basis and their symptoms, temperature and SpO2 levels were thus monitored. If no improvement was ascertained, the next prescribed medicines were sent by health workers to the person's home. The patients admitted to a CCC were given a first prescription after in-person consultation and were followed up daily until their discharge from the CCC, and thereafter at home telephonically for all the monitored parameters. The medicines were procured from a GMP-certified company. Ethical approval was obtained from the Nehru Homoeopathic Medical College and Hospital research ethics committee (letter number F/No5(11)/93/NHMC/Academic/PG 2007/1913), on June 2, 2020. Patients who were willing and gave verbal consent were prescribed homeopathic medicines.

Participants

All patients, of either sex, having mild, moderate disease or severe disease were considered. Mild disease was categorized as upper respiratory tract symptoms (and/or fever) without shortness of breath or hypoxia; moderate disease as respiratory rate >24/min, breathlessness and/or SpO2 90% to 93% on room air; severe disease as respiratory rate >30/min, breathlessness and/or SpO2 <90% on room air.[16,17] Those with co-morbidities were also included in the study. The information related to the identity of the patients was kept confidential.

Variables

The variables comprise the demographic profile and the clinical presentation of patients. Homeopathic medicines and their indications were used as prognostic factors.

Data Source

Doctors who had treated COVID-19 positive cases during the second wave were asked to complete the customized Excel spreadsheet which contained 75 fields covering the spectrum of symptoms with respect to the second wave. It also contained symptoms related to mental and emotional states, e.g., sadness, confusion, restlessness and anxiety, to record the fear and worry associated with this disease.[24,25] The spreadsheet also contained columns for detailed follow-ups and outcome after 1 week of treatment. Doctors followed up telephonically those patients who were in home isolation.

In every follow-up, the patient was asked about the change in intensity of each symptom and his or her general well-being, as is done in any homeopathic case follow-up in a regular setting. The Outcome in Relation to Impact on Daily Living (ORIDL) scale, a validated measure of patient-rated outcomes, and which ranges from –4 to +4, was used for the assessment of patients at each follow-up.[26] This assessment scale is being used as standard practice at IDGHCs in respect of all patients. The scale was adopted there in the year 2019, well before the COVID-19 pandemic.

To ensure consistency in data and to reduce bias, online meetings with all doctors were organized on a regular basis. Each doctor filled in his/her cases in the Excel spreadsheet, which was mailed to the data analysis team. After collection of data from all the doctors, cleaning and compilation of data was carried out. Establishing causality is an important prerequisite for PFR.[18] Cases with inadequate information, or in which a causal relationship between the medicine and the outcome could not be established, were therefore excluded from the analysis. A set of selection criteria based on the Modified Naranjo Criteria (MNC)[27] and our previous study on COVID cases[19] was adopted, wherein only four out of the 10 domains of MNC were considered. The criteria were:

Domain 1 and 5 of MNC: only those cases with a reported ORIDL outcome of +3 or +4 were selected as these indicate that there was marked improvement in main complaints and overall well-being, which were considered as desirable effects of the homeopathic medicine.

Domain 2 of MNC: only those cases where improvement started within 24 hours of medicine intake and the desired recovery on ORIDIL scale was reported within 7 days were included. This was done to eliminate cases with spontaneous recovery as per our experience during the first wave, wherein mild to moderate cases were known to improve spontaneously in 10 to 14 days.

Domain 10 of MNC: cases were included where there was continuous improvement seen after repeating the doses of the selected medicine.

Cases with inadequate information, asymptomatic patients (wherein it was not possible to make any assessment), cases which showed no improvement, and cases in whom causality could not be established were excluded (►Fig. 1).

Statistical Methods

Analysis was based on calculation of LR to improve the reliability of prescriptions. It is expressed in a statistical formula known as Bayes' theorem: posterior odds = LR × prior odds, where LR = prevalence in the target population/prevalence in the remainder of the population. The target population is the population in which the medicine has a curative effect.[28]

The LR of a symptom indicates a change in the chance of improvement by that medicine when that symptom is present in a patient. If LR is > 1, it implies that the patient is more likely to improve with that medicine in the presence of that symptom.[19,28] The higher the LR, the more strongly is the medicine indicated for that symptom.

In epidemic diseases, the symptoms that are typical for the disease (common symptoms) have a high prevalence and thus lower LRs. LR = 1.3 or more was considered meaningful. A
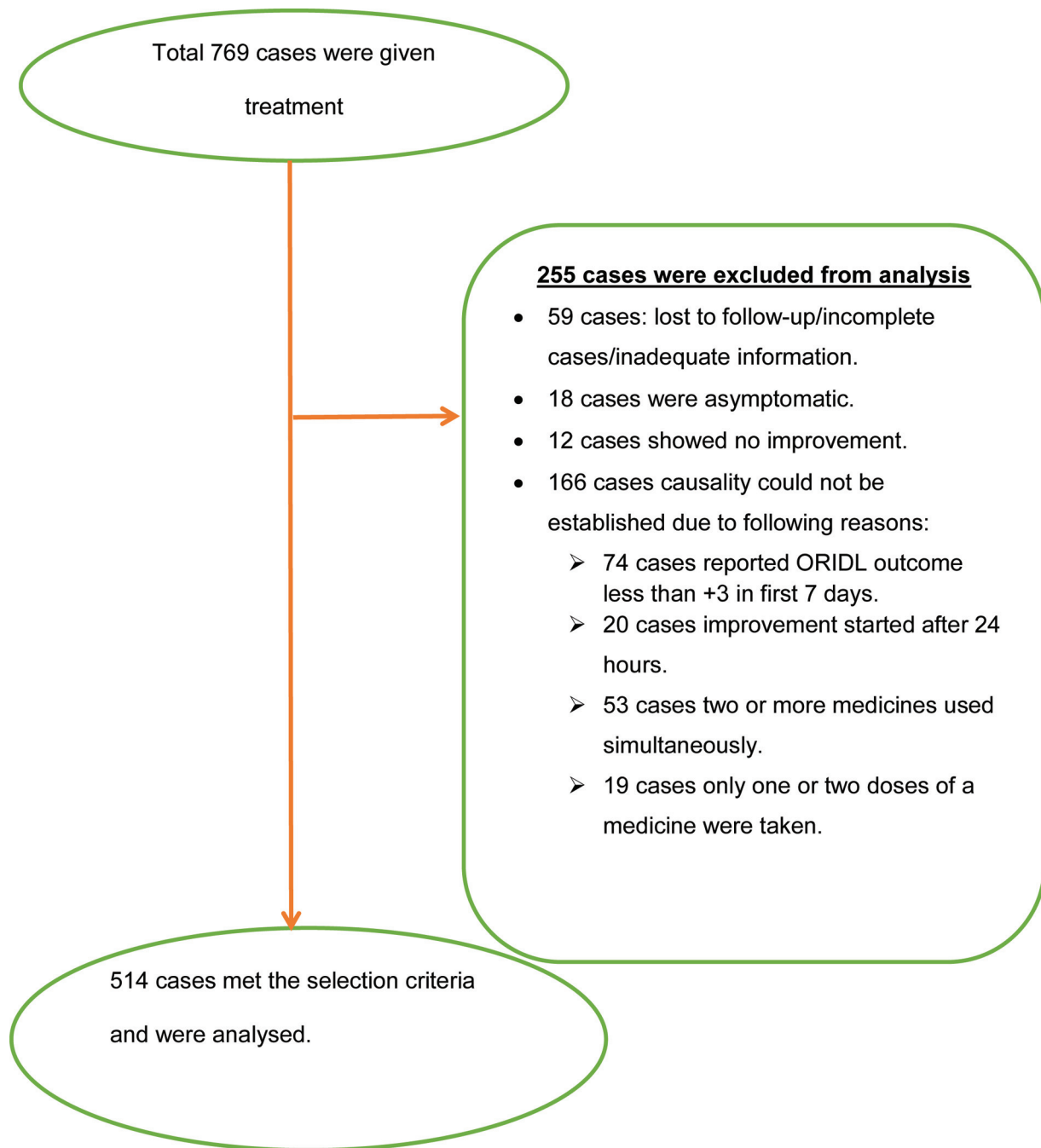
Fig. 1 Flowchart of the study.

combination of such symptoms indicates the homeopathic medicine.

Results

A total of 769 COVID-19 patients were treated with add-on homeopathic medicines. Most cases improved and there was no adverse reaction. After applying the selection criteria, 514 cases were available for analysis. Out of these 514 selected cases, 467 (90%) were in home isolation while 47 (10%) were in COVID Care Centres.

Out of 769 cases, 255 were excluded from analysis due to various reasons such as inadequate follow-up (59 cases),

being asymptomatic (18 cases), or causality not being established (166 cases) (►**Fig. 1**).

Two hundred and sixty-seven patients were male and 247 were female (►**Table 1**). The majority of patients, 413 in number, were in the age group of 18 to 60 years, while 49 were below 18 years and 52 were more than 60 years of age, the youngest being 10 months and the eldest 82 years. Co-morbidity was present in 105 patients. A total of 459 cases were mild, 44 were moderate, and 11 cases were severe.

Of these, 70 patients took only homeopathic treatment while 444 used conventional symptomatic treatment as well as homeopathy. As per the revised COVID-19 guidelines, mild cases can be discharged after 10 days of symptom onset and no

Table 1 Demographic data ($n = 514$)

		n	%
Gender	Male	267	51.95
	Female	247	48.05
Age group	<18	49	9.53
	18–60	413	80.35
	>60	52	10.12
Co-morbidity	Present	105	20.43
	Absent	409	79.57
Severity	Mild	459	89.30
	Moderate	44	8.56
	Severe	11	2.14
Medicine taken	Only homeopathy	70	13.62
	Homeopathy and conventional	444	86.38
COVID vaccine taken	Single dose	61	11.87
	Two doses	37	7.20
	Not vaccinated	416	80.93
Status of COVID test	RT-PCR positive	347	67.51
	RAT positive	153	29.77
	RT-PCR negative but symptoms	14	2.72

Table 2 Presenting complaints/symptoms (for symptoms up to 10 cases)

Symptom	Number of cases	%
Cough	321	62.45
Fever	312	60.70
Muscle/bone pain	244	47.47
Throat pain	228	44.36
Thirst increased	218	42.41
Dry cough	213	41.44
Headache	202	39.30
Dry mouth/throat	197	38.33
Loss of appetite	161	31.32
Fatigue	163	31.71
Loss of taste and/or smell	153	29.77
Anxiety/fear	137	26.65
Perspiration	112	21.79
Chill	115	22.37
Productive cough	108	21.01
Coryza	106	20.62
Restless	92	17.90
Chest discomfort	88	17.12
Nose blocked	83	16.14
Thirstless	81	15.76
Dyspnea	79	15.37
Sleeplessness	67	13.04
Diarrhea	63	12.26
Sadness	52	10.12
Sneezing	52	10.12
Pneumonia	51	9.92
Constipation	42	8.17
Nausea	37	7.20
Abdominal pain	33	6.42
Confusion	15	2.92
Conjunctivitis	10	1.95

fever for 3 days, with advice to isolate at home and self-monitor their health for a further 7 days. Moderate cases with resolution of clinical symptoms, absence of fever without antipyretics, resolution of breathlessness and oxygen saturation being maintained above 95% for the next 3 days without supplementary oxygen, were able to be discharged. There was no requirement then for testing prior to discharge.[16]

The most common complaints were cough (321 cases), fever (312 cases), myalgia (244 cases), sore throat (228 cases), loss of taste and/or smell (153 cases) and anxiety (137 cases). In the second wave, more patients complained of headache (202), dryness of mouth (197), chest discomfort (88), dyspnea (79) and pneumonia (51). Gastrointestinal symptoms, e.g., anorexia (161), diarrhea (63), nausea (37) and abdominal pain (33), were also more common than in the first wave. A symptom, conjunctivitis, was also seen in 10 cases (►**Table 2**).

Thirty-nine medicines in varying potencies were prescribed, usually starting from 30C (►**Table 3**). The medicines were repeated as per the need of a case, and usually three to four times daily. In some cases, they were repeated more frequently. The most prescribed medicine was *Bryonia alba (Bry)* in 161 cases, followed by *Arsenicum album (Ars)* in 98 cases, *Pulsatilla nigricans (Puls)* in 51 cases and *Belladonna (Bell)* in 31 cases. *Gelsemium sempervirens (Gels)* was given in 27 cases, *Hepar sulphuris (Hep)* in 22, and *Phosphorus (Phos)* in 17 cases. *Rhus toxicodendron (Rhus-t)* and *Mercurius solubilis (Merc)* were given in 14 cases each. Some less frequently used medicines, e.g., *Antimonium tartaricum,*

Nux vomica, Lachesis, Eupatorium perfoliatum, Carbo vegetabilis and *Kali bichromicum*, were also prescribed with benefit, though the number of such cases was low (►**Table 3**).

Cases that are "false positive cures", i.e., causality wrongly attributed to the remedy, cause underestimation of LR of a specific symptom for a specific remedy.[27] Therefore, only those cases that fulfilled the specific selection criteria were analyzed and LR was calculated only in respect of frequently prescribed medicines for frequently occurring symptoms (►**Table 4**). LR >1 indicates that there is an increased chance that a medicine will be effective if a certain symptom is present. By calculating LR, a comparative could be drawn, symptom wise, between these nine medicines for COVID-19 cases. A blank in ►**Table 4** indicates that there was no patient

Table 3 Medicines prescribed as an adjunct therapy

Medicine	Number of patients improved
Bryonia alba	161
Arsenicum album	98
Pulsatilla nigricans	51
Belladonna	31
Gelsemium sempervirens	27
Hepar sulphuris	22
Phosphorus	17
Rhus toxicodendron	14
Mercurius solubilis	14
Antimonium tartaricum	8
Nux vomica	7
Lachesis	7
Carbo vegetabilis	5
Natrum muriaticum	5
Camphora officinarum	4
Eupatorium perfoliatum	4
Causticum hahnemanni	4
Kali bichromicum	3
Calcarea carbonica	3
Ignatia amara	3
Chininum arsenicosum	3
Spongia tosta	2
Sulphur	2
Phytolacca decandra	2
Magnesia muriatica	2
Iodium	2
Rumex crispus	1
Veratrum viride	1
Stannum metallicum	1
Aconitum napellus	1
Crotalus horridus	1
Argentum nitricum	1
Natrum arsenicum	1
Chelidonium majus	1
Wyethia	1
Calcarea sulphurica	1
Natrum sulphuricum	1
Pyrogenium	1
Ipecacuanha	1

responding well to that remedy when the symptom was present.

Ars had relatively high LR for symptoms such as coryza (1.52), sneezing (1.89), restlessness (1.73) and anxiety (1.40),

and for GI symptoms like diarrhea (1.83) nausea (1.80) and abdominal pain (1.85).

Bell had relatively high LR for the symptoms headache (1.62) and conjunctivitis (3.90).

Bry had relatively high LR for the symptoms dry cough (2.09), dryness of mouth (1.73), chest discomfort (1.32), constipation (3.95), increased thirst (2.79) and conjunctivitis (1.46).

For fever, *Bell*, *Bry*, *Gels* and *Phos* all had LR >1, but highest LR was for *Merc* (1.43).

Gels had high LR for the symptoms headache (1.87), chill (3.35), sneezing (1.92), anorexia, fatigue (1.43), sleeplessness (1.45), coryza (2.09) and thirstlessness (7.59).

Hep had high LR for the symptoms throat pain (1.57) and productive cough (1.79).

Merc showed meaningful LR for the symptoms throat pain (1.47), productive cough (2.10), fever (1.43), chills (3.40), myalgia (1.53), increased perspiration (4.69), chest discomfort (2.15), dyspnea (2.41), sleeplessness (1.67) and fatigue (2.09).

Phos had the highest LR for pneumonia (5.44), dyspnea (3.76), chest discomfort (3.75) and productive cough (2.66). It showed meaningful LR for the symptoms fatigue (1.71) and increased perspiration (1.65).

Puls had the highest LR for loss of taste/smell (2.69) and thirstlessness (8.86). It had high LR for the symptoms productive cough (2.19), anorexia (1.44) and sadness (1.90).

Rhus-t symptoms with meaningful LR were restlessness (3.87), coryza (2.4), sleeplessness (1.67), anxiety (1.35) and blockage of nose (1.34).

Discussion

In an epidemic, rare and peculiar symptoms are difficult to find. Therefore, PFR assumes importance wherein symptoms are regarded as factors, which helps in establishing the relationship between specific symptoms (prognostic factors) and medicines.[19] Even common symptoms of a disease can assume importance if the LR of common symptoms is high for a specific medicine. A combination of such symptoms becomes prescribing indications (prognostic factors) for that medicine.

By using PFR, the most likely indications of medicines for a condition can be ascertained and also a comparison between medicines can be drawn. For example, in cases with conjunctivitis in COVID-19, both *Bell* and *Bry* acted well but the LR for *Bell* is higher (3.90) as compared with *Bry* (1.46). Also, headache was more marked in *Bell*: thus, it may help in differentiating between the two medicines.

Both *Ars* and *Gels* were indicated by the symptoms anxiety, coryza, sneezing and sleeplessness, but chill was marked in *Gels* though insignificant in *Ars*. Restlessness was marked in *Ars*, not in *Gels*. Also, thirstlessness was a differentiating feature.

Merc had throat pain (1.47) and productive cough (2.10) like *Hep*, but other symptoms like fever, chills (3.40), myalgia (1.53), increased perspiration (4.69), chest discomfort

Table 4 Likelihood ratio calculations for nine medicines for symptoms

Symptoms	Count	Ars	LR Ars	Bell	LR Bell	Bry	LR Bry	Gels	LR Gels	Hep	LR Hep	Merc	LR Merc	Phos	LR Phos	Puls	LR Puls	Rhus-t	LR Rhus-t
	514	98		31		161		27		22		14		17		51		14	
Cough	321	51	0.80	11	0.55	124	1.38	11	0.64	11	0.79	9	1.03	15	1.43	31	0.97	6	0.68
Fever	312	51	0.83	23	1.24	105	1.11	19	1.17	11	0.82	12	1.43	11	1.07	26	0.83	8	0.94
Muscle/bone pain	244	42	0.88	8	0.53	88	1.24	18	1.44	7	0.66	10	1.53	6	0.74	19	0.77	14	2.17
Throat pain	228	37	0.82	17	1.26	75	1.07	16	1.36	15	1.57	9	1.47	4	0.52	17	0.73	7	1.13
Thirst increased	218	45	1.10	5	0.37	122	2.79	0		1	0.10	10	1.72	6	0.83	3	0.13	4	0.67
Dry cough	213	27	0.62	7	0.53	104	2.09	8	0.70	3	0.32	3	0.51	6	0.85	10	0.45	4	0.68
Headache	202	31	0.77	19	1.62	70	1.16	19	1.87	4	0.45	2	0.36	7	1.05	15	0.73	7	1.28
Dry mouth/throat	197	26	0.65	6	0.49	87	1.73	10	0.96	3	0.35	10	1.91	8	1.24	20	1.03	5	0.93
Loss of appetite	161	30	0.97	7	0.71	51	1.02	14	1.72	7	1.02	1	0.22	2	0.37	22	1.44	2	0.45
Fatigue	163	37	1.25	1	0.10	43	0.79	12	1.43	3	0.42	9	2.09	9	1.71	12	0.72	5	1.13
Loss of taste and/or smell	153	20	0.64	4	0.42	43	0.86	7	0.86	4	0.60	6	1.46	4	0.78	35	2.69	4	0.96
Anxiety/fear	137	34	1.40	2	0.23	33	0.70	12	1.73	2	0.33	4	1.07	4	0.88	15	1.12	5	1.35
Perspiration	112	16	0.71	1	0.14	32	0.88	5	0.84	5	1.05	13	4.69	6	1.65	11	0.99	3	0.98
Chill	115	18	0.79	5	0.71	21	0.49	18	3.35	4	0.81	10	3.40	3	0.78	14	1.26	3	0.96
Productive cough	108	24	1.21	4	0.60	20	0.50	3	0.52	8	1.79	6	2.10	9	2.66	21	2.19	2	0.67
Coryza	106	28	1.52	1	0.15	27	0.75	11	2.09	1	0.21	2	0.69	2	0.56	12	1.16	6	2.14
Restless	92	27	1.76	4	0.71	25	0.82	3	0.61	2	0.50	1	0.39	1	0.32	4	0.41	9	3.87
Chest discomfort	88	13	0.74	0		33	1.32	4	0.86	1	0.26	5	2.15	10	3.75	6	0.66	0	
Nose blocked	83	15	0.94	6	1.21	22	0.79	6	1.41	3	0.84	1	0.44	4	1.48	9	1.10	3	1.34
Thirstless	81	4	0.22	2	0.39	1	0.03	24	7.59	1	0.28	1	0.45	2	0.74	40	8.86	2	0.90
Dyspnea	79	16	1.08	2	0.40	26	1.08	2	0.47	2	0.58	5	2.41	9	3.76	2	0.24	2	0.93
Sleeplessness	67	15	1.22	0		15	0.63	5	1.45	2	0.69	3	1.67	4	1.86	8	1.23	3	1.67
Diarrhea	63	19	1.83	3	0.78	14	0.63	3	0.90	1	0.36	1	0.58	2	0.96	6	0.96	1	0.58
Sadness	52	12	1.27	0		15	0.89	1	0.35	1	0.44	1	0.70	2	1.17	9	1.90	1	0.70
Sneezing	52	16	1.89	2	0.62	9	0.46	5	1.92	1	0.44	1	0.70	1	0.57	4	0.76	1	0.70
Pneumonia	51	6	0.57	1	0.31	15	0.91	2	0.74	1	0.45	2	1.46	8	5.44	5	0.99	1	0.71
Constipation	42	2	0.21	0		27	3.95	1	0.44	0		1	0.87	0		1	0.22	1	0.87
Nausea	37	11	1.80	0		6	0.42	0		0		0		0		2	0.52	3	3.15
Abdominal pain	33	10	1.85	2	1.01	4	0.30	2	1.16	0		1	1.12	1	0.91	2	0.59	1	1.12
Confusion	15	2	0.65	0		5	1.10	1	1.29	2	3.44	1	2.55	0		2	1.40	0	
Conjunctivitis	10	1	0.47	2	3.90	4	1.46	0		0		0		0		1	1.01	0	

Table 5 Likelihood ratio comparison for symptoms for four medicines used in first wave (Wave 1) as well as in second wave (Wave 2) of COVID-19

Symptoms	LR *Ars*		LR *Bry*		LR *Gels*		LR *Puls*	
	Wave 2	Wave 1	Wave 2	Wave 1	Wave 2	Wave 1	Wave 2	Wave 1
Fever	0.83	0.99	1.11	0.99	1.17	1.96	0.83	1.02
Muscle/bone pain	0.88	1.02	1.24	1.21	1.44	1.90	0.77	0.38
Throat pain	0.82	0.98	1.07	1.04	1.36	0.59	0.73	0.52
Thirst increased	1.10	1.66	2.79	1.88		0.15	0.13	0.23
Dry cough	0.62	0.68	2.09	2.08	0.70	0.79	0.45	0.38
Headache	0.77	0.61	1.16	1.44	1.87	1.42	0.73	1.27
Dry mouth/throat	0.65	1.05	1.73	2.05	0.96	0.70	1.03	1.06
Loss of appetite	0.97	0.88	1.02	1.05	1.72	2.15	1.44	1.46
Fatigue	1.25	1.38	0.79	0.91	1.43	1.92	0.72	0.47
Anxiety/fear	1.40	2.28	0.70	0.38	1.73	2.12	1.12	0.61
Perspiration	0.71	0.41	0.88	1.84	0.84	4.04	0.99	
Chill	0.79	0.49	0.49		3.35	10.1	1.26	2.18
Productive cough	1.21	0.85	0.50	0.61	0.52	0.95	2.19	1.97
Coryza	1.52	3.07	0.75	0.49	2.09		1.16	0.90
Chest discomfort	0.74	0.89	1.32	1.88	0.86	0.72	0.66	1.09
Nose blocked	0.94		0.79	2.15	1.41	0.72	1.10	2.32
Thirstless	0.22	0.29	0.03	0.46	7.59	7.35	8.86	2.86
Dyspnea	1.08	0.65	1.08	1.76	0.47	1.44	0.24	0.66
Sleeplessness	1.22	1.72	0.63	0.64	1.45	1.31	1.23	0.46
Diarrhea	1.83	0.95	0.63	0.70	0.90	0.59	0.96	0.90
Sneezing	1.89	3.07	0.46	0.31	1.92		0.76	
Constipation	0.21	0.25	3.95	6.56	0.44		0.22	0.73
Nausea	1.80	1.09	0.42	1.09		0.84	0.52	2.77
Abdominal pain	1.85	1.05	0.30	1.05	1.16	1.12	0.59	1.69

Note: This comparison is only for four medicines: *Ars, Bry, Gels* and *Puls.*

(2.15), dyspnea (2.41), sleeplessness (1.67) and fatigue (2.09), were also marked, which were absent or not significant in *Hep.*

Merc is somewhat similar to *Gels* but symptoms like sneezing, coryza and headache are more prominent in *Gels* and less so in *Merc. Merc* is thirsty (1.72) whilst *Gels* is thirstlessness (7.59). *Merc* worked well in pneumonia (1.46), unlike *Gels* (0.74). Pneumonia indicated *Phos* more than *Merc.* Both medicines showed the symptoms fatigue, increased perspiration, chest discomfort and sleeplessness, but the symptoms loss of taste/smell and fever with chill were present in *Merc,* unlike *Phos.* The symptom nose blockage was seen in *Phos* (1.48) and *Gels* (1.41). Interestingly therefore, LR also helps to confirm the symptomatology of a remedy.

Indications of some of the medicines found useful in the second wave were analogous to those in the first wave:[19] e.g., *Ars* was most indicated by anxiety and running nose during the first wave as well as in the second wave. *Bry* was indicated in dry cough, with increased thirst, constipation

and dryness of mouth, in both the waves. *Gels* was indicated for the symptoms chills, fatigue, decreased thirst, myalgia and decreased appetite in both the waves. *Puls* was more indicated by the symptoms productive cough and thirstlessness (►**Table 5**). However, in this study some symptoms for these medicines were more marked: for example, *Ars* in GI symptoms like diarrhea (1.83), nausea (1.80) and abdominal pain (1.85). Some additional indications for these medicines could also be elucidated: for example, *Gels* for the symptom coryza (2.09) and *Puls* for the symptom sadness (1.90) (►**Table 4**). Also, a greater number of medicines were used in the second wave as compared with the first. A new indication in the second wave was the combination of headache and conjunctivitis for *Bell.*

In this study, homeopathic medicines have shown encouraging responses in an integrated as well as a sole treatment regimen and even in cases with co-morbidities. No adverse reaction was observed for any of the medicines. However, since there were smaller numbers of severe cases (11) and they were under constant oxygen support in the CCC, the

effectiveness of homeopathy in such cases needs to be further explored.

Successful prescriptions are based on careful individualization of symptoms, either for an individual patient or collectively in epidemic outbreaks.[29] Homeopathic medicines have shown promising results for epidemic diseases such as cholera, influenza, dengue and Japanese encephalitis.[30]

Results of this study show that homeopathy can offer support as an adjunct therapy, along with conventional drugs, in clinical management in the prevailing COVID-19 pandemic. It also confirms the prognostic factors of four medicines used in our previous study.[19] Prescribing indications of five more medicines have been ascertained in this study. The results of this study may be helpful in prescribing for COVID-19 cases in future. Also, it may help in the preparation of a Materia Medica and repertory on COVID-19. Since conjunctivitis was a new symptom in the second wave, the relationship between conjunctivitis and *Bell* may be investigated in future studies.

Limitation

Since patients were also taking conventional medicines, an overestimation of the causal relationship between clinical improvement and homeopathic medicines cannot be ruled out. Though the selection criteria used in this study make a causal relationship more likely, they do not exclude the possibility of context effects, spontaneous recovery, placebo effects, etc. Since the number of severe cases was small, the role of confounding factors such as pre-hospitalization health status and underlying medical problems could not be determined.

Conclusion

Add-on use of homeopathic medicines has shown encouraging results in the second wave of COVID-19 for patients in home isolation or at integrated COVID care facilities. The prognostic factors of *Bry, Ars, Puls* and *Gels,* as elucidated in the first wave, were confirmed in this study, while the prescribing indications of new medicines *Bell, Hep, Phos, Rhus-t* and *Merc* were identified using PFR. A potentially increased indication for *Bell* was discovered in the second wave. Further research is required to be undertaken with the group of these identified medicines in future waves of COVID-19.

Highlights
- The second wave of COVID-19 in India had increased intensity, a prolonged course, and presented the new symptom conjunctivitis.
- Homeopathic medicines were used as an adjunct to conventional therapy.
- The prognostic factors of nine medicines were discerned.
- Prognostic factors of the medicines *Bry, Ars, Puls* and *Gels*, used in the previous outbreak, were confirmed in the second wave.

- Prescribing indications of five more medicines – *Bell, Hep, Phos, Rhus-t,* and *Merc* – were recognized.
- *Bell* was prescribed more often in the second wave because of the higher prevalence of conjunctivitis.

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