

Original Research Article

Evaluating effects of allo-vedic preparation Raj Nirwan Bati on symptomatic cases of COVID-19 at a tertiary level health care facility in rural setting of northern India

Raj Kumar¹, Ramakant Yadav², Ramakant Rawat³, Naresh P. Singh^{4*},
Indra K. Sharma⁵, Prashant Yadav⁶

¹Department of Neurosurgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

²Department of Neurology, ³Department of Internal Medicine, ⁴Department of Community Medicine, ⁵Department of Pediatrics, ⁶Department of Respiratory Medicine, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India

Received: 15 September 2021

Revised: 08 October 2021

Accepted: 12 October 2021

*Correspondence:

Dr. Naresh P. Singh,

E-mail: nareshpalsingh@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The present pandemic of COVID-19 has created a huge pressure on the current health system of the world as the burden is increasing exponentially day by day. Study evaluated the effect of the novel allo-vedic formulation named Raj Nirwan Bati (RNB) on the clinical symptoms, microbiological, bio-chemical, haematological and radiological profile of patients of COVID-19.

Methods: Prospective single arm, non-randomized clinical trial was conducted which enrolled 40 reverse transcriptase-polymerase chain reaction (RT-PCR) confirmed patients of severe acute respiratory syndrome corona virus-2 (SARS-CoV-2). Each patient was given one dosage of RNB twice a day for 10 days. Patients were evaluated on the clinical symptoms, microbiological, bio-chemical, haematological and radiological profile of patients of COVID-19. Cochran's Q tests was used to assess statistical significance.

Results: The study revealed that 31 (77.5%) of the COVID-19 cases were having mild, 6 (15%) moderate and 3 (7.5%) having severe form of illness. The association between absence of clinical symptom (fever, cough, breathlessness, sore throat, fatigue and myalgia) and the day of evaluation (first, fifth and tenth day) after start of RNB intervention was found to be statistically significant ($p < 0.001$, $p < 0.001$, $p = 0.002$, $p < 0.001$, $p < 0.001$ and $p < 0.001$) respectively. Thirty (75.0%) of the cases on RNB intervention became negative for SARS-CoV-2 after day 5 on naso-pharyngeal and oropharyngeal RT-PCR testing ($p < 0.001$). Statistically significant association was observed only for changes in proportion of cases with elevated lactate dehydrogenase (LDH) values and C-reactive protein (CRP) positive from day 1 to day 10 of RNB intervention ($p < 0.001$).

Conclusions: RNB may be considered a drug to fight against COVID-19.

Keywords: COVID-19, Ayurvedic medicine, SARS-CoV-2, RT-PCR

INTRODUCTION

The year 2020 became the most challenging year, specifically, for the fraternity of medical field in purview of the present pandemic of corona virus disease 2019

(COVID-19). From the Ayurvedic point of view, COVID-19 is a *janapadodhwansa vikara* (epidemic disease). *Janapadodhwansa* is a situation where the environment - air, water, land and seasons - is vitiated, causing a simultaneous manifestation of a disease among large

populations (epidemic), and destroying human habitations.¹

Although efforts have been initiated in scientific research to determine and formulate the treatment of COVID-19, scientists are still not in a position to win the invisible war against the severe acute respiratory syndrome-corona virus-2 (SARS-CoV-2). In a chain of researches conducted at University of China till now, about 30 drugs have been identified as possible treatment options for the COVID-19.² Another research on 47 drugs, with mechanism of action mainly against protease of SARS-CoV-2, has found 13 drugs having good potential but these drugs are still in the research phase and no effective treatment is yet available for COVID-19 disease.³

There is a felt need for research on various treatment options available in the indigenous system of medicine. Despite a wealth of anecdotal and written knowledge, India has never tested Ayurveda in large clinical trials before. Few ayurvedic (Indian system of medicine) preparations have earlier been proven to fight against many viruses and play an important role in boosting the immunity of the human body. In India there is precedence of treating the chikungunya virus epidemic with Ayurveda and Siddha medicines.⁴

Recently a similar research conducted on microbiologically confirmed COVID-19 patients in rural setting in India reported that a novel Ayurvedic herbo-mineral preparation named *Raj Nirwan Bati* (RNB) with about 11 ingredients was found to provide considerable symptomatic relief cum cure and making as many as 80% of the COVID-19 cases negative within five days on reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2.⁵ This study was aimed to evaluate the effect of an allo-vedic preparation RNB on the clinical symptoms, bio-chemical profile, haematological profile, radiological profile and its role in producing relief cum cure to COVID-19 cases.

METHODS

Study design

In view of the limited available scientific knowledge about the disease, a single arm, non-randomized clinical trial was conducted on microbiologically RT-PCR confirmed and symptomatic COVID-19 patients. These cases were admitted and being treated at the dedicated COVID-19 hospital, specifically earmarked for it, at a tertiary level health care facility in a Medical University in rural setting of the state of Uttar Pradesh in Northern India. At the time of admission, the patients were categorized into three groups, namely mild, moderate, and severe illness. In mild symptomatic group, those cases were included who had symptoms of fever, cough and other clinical symptoms without dyspnoea and saturation of peripheral oxygen (SpO₂) >94%. Symptomatic cases having fever and cough and other clinical symptoms with dyspnoea and

SpO₂ >94% were taken in to moderate symptomatic group. Symptomatic cases that had fever and cough with dyspnoea and SpO₂ between 90-94% requiring intensive care unit admissions were included in severe group.

Sample size

Among a total of 205 cases of COVID-19 hospitalized for treatment, only 40 cases could meet the criteria of present study during the study period of two months from May-2020 to June-2020. Hence, census sampling method was used to recruit the cases of COVID-19 positive patients who fulfilled the inclusion criteria of the study for the intervention.

Inclusion and exclusion criteria

Symptomatic cases (fever, cough, breathlessness, fatigue, myalgia, chest tightness, headache, diarrhoea, vomiting, abnormal sleep pattern, loss of appetite, loss of taste and smell sensations) aged 18 years or more and admitted with positive RT-PCR test for SARS-CoV-2 were included in the present study. Patients who refused to provide informed written consent to participate in the study, asymptomatic cases, critically ill patients (SpO₂ <90% with shock or altered sensorium) requiring ventilatory support for management, patients with deranged renal function (eGFR <60 ml/minute), pregnant and lactating females were excluded from the study. However, patients with other comorbidities were included in the study group.

Drug formulation for the intervention

The composition of the novel allo-vedic preparation, RNB was formulated using eleven constituents which are namely, highly purified and processed mercury (paara), processed sulphur (gandkak), highly purified and almost nano-particle of gold (sona) and silver (chandi), clamina perpeta, arsenic trioxide (hartal bhasma), black pepper (*Piper nigrum*, kaali mirch), *Artemisia nilagirica* (nag damanti, snake plant), *Carum copticum* (celery, azwaayin), zinc containing compound (kharpar) and mahamash oil (Niramish). The term allo-vedic was coined because we followed the principles and gadgets of modern system of medicine (allopathy) and the ingredients of this RNB were as per recommendations in materia medica of Ayurveda system of medicine and within safe, recommended permissible limit.

Some of the Ayurvedic treatments have been proven to increase innate immunity and this was the rationale behind choosing each ingredients of Raj Nirwan. All components of this drug were processed with high refinement and expertise as per the recommendations made in the ancient Indian system of medicine by a dedicated and established expert of ancient sciences. The expert was chosen following a thorough evaluation of his knowledge of the ancient system of medicine and who had adopted this system as a family tradition. The preparation was very laborious, time consuming and skill based (almost difficult

and harmful, if prepared by untrained hands). Thus, prepared allo-vedic formulated RNB was used as an interventional drug.

Methodology

The present study used RNB, which was given to all three groups of patients (patients with mild/moderate/severe symptoms). Each patient was given one dosage of 125 milligrams tablet empty stomach twice a day with 5 ml of natural honey for 10 days and continued up to 12 days depending on severity. Along with this RNB intervention, standard treatment was given to each patient as per the current knowledge or national treatment guidelines laid down from time to time by competent higher authorities. Other than RNB these cases were given vitamin B-complex with zinc and vitamin C.

Assessment of outcome variables

Clinical assessment of study subjects was done by qualified and COVID-19 trained doctors daily. Adverse drug reactions, if any, were observed regularly by faculty physician. All the vital parameters were monitored daily. Standard laboratory investigations included haemoglobin level, total leukocyte count, differential leukocyte count, platelet count, serum glutamic pyruvic transaminase (SGPT), serum glutamic-oxaloacetic transaminase (SGOT), serum urea, serum creatinine, C-reactive protein (CRP), serum lactate dehydrogenase (LDH), creatine phosphokinase (CPK) were done as baseline investigation on day of start of RNB intervention followed by repeat investigations on day 5 and day 10 and as and when required. Microbiological test in the form of RT-PCR for COVID-19 and chest X-ray PA view were done for each patient on the day of the start of RNB, 5th and 10th day for micro-biological and radiological evaluation respectively during the course of intervention.

Statistical analysis

The data thus collected were first entered on Microsoft excel spreadsheet and analysed using statistical package for the social sciences (SPSS) software, version 25 (IBM Corp., Chicago, USA). Statistical significance was assessed using Cochran's Q test and $p < 0.05$ at 95% confidence interval was considered statistically significant.

Ethical consideration

Informed written consent was obtained from each participant at the time of their enrolment in the study. Ethical clearance was taken from the ethics committee of the University before the commencement of the study. Study was also enrolled in clinical trials registry-India (CTRI), Indian Council of Medical Research- National Institute of Medical Statistics, New Delhi with CTRI number CTRI/2020/06/025852.

RESULTS

Findings of the present study revealed that almost half (47.5%) of the study participants were young adults (21-40 years) and majority (77.5%) were males. Six (15%) of the cases were above 60 years of age. Table 1 also reveals that according to severity of COVID-19 illness, majority (77.5%) were having mild illness, followed by moderate (15.0%) and severe (7.5%). It was also observed that 10 out of 40 studied cases had one or the other comorbidities like diabetes, hypertension, bronchial asthma, coronary artery disease, chronic liver disease or even mass in lung.

Table 1: Demographic and clinical profile of the COVID-19 cases (N=40).

Variables	n (%)
Age-groups (in years)	
21-40	19 (47.5)
41-60	15 (37.5)
61-80	6 (15.0)
Mean±SD	43.53±14.75
Gender	
Male	31 (77.5)
Female	9 (22.5)
Severity of COVID-19 illness	
Mild	31 (77.5)
Moderate	6 (15.0)
Severe	3 (7.5)
Cases with comorbidities* (n=10)	
Hypertension	2 (5.0)
Diabetes	5 (12.5)
Diabetes and hypertension	1 (2.5)
Coronary artery disease/ischemic heart disease	2 (5.0)
Chronic liver disease	1 (2.5)
Bronchial asthma	1 (2.5)
Right lung mass	1 (2.5)

*Multiple findings in cases

Table 2 depicts the effect of RNB intervention on various symptoms during the course of intervention on the basis of severity of illness (COVID-19). It was observed that on day 1 of start of RNB intervention, 23 cases (57.5%) had fever which was reduced to 6 cases (15%) on day 5 with a median time to get relieved from fever as 4.5 days with range of 7 days. Similarly, improvement in other symptoms like cough from 35 cases (87.5%) to 8 cases (20.0%), breathlessness 9 cases (22.5%) to 6 cases (15.0%), sore throat from 18 cases (45.0%) to 6 cases (15.0%), fatigue from 33 cases (82.5%) to 8 cases (20.0%) and myalgia from 13 cases (32.5%) to 6 cases (15.0%) on day 1 and day 5 respectively was observed. In majority of the cases, almost complete symptomatic relief was seen by day 10 of RNB intervention; more so in cases with mild and moderate illness. The association between the day of evaluation after RNB intervention and absence of clinical symptom (fever, cough, breathlessness, sore throat, fatigue

and myalgia) was found to be statistically significant ($p<0.001$, $p<0.001$, $p=0.002$, $p<0.001$, $p<0.001$ and $p<0.001$) respectively. Table 3 reveals that 30 (75.0%) of the cases on RNB intervention became negative for SARS-CoV-2 after day 5 on naso-pharyngeal and oro-pharyngeal RT-PCR testing and subsequently all the study cases turned negative on day 12 of RNB intervention ($p<0.001$). There was a substantial increase in the haemoglobin level of the cases during intervention as the proportion of non-anaemic cases raised from 37.5% to 47.5%. Normal neutrophil-lymphocyte ratio ($NLR<2.93$) increased from 22 cases (55%) to 29 cases (72.5%), thrombocytopenia (platelets <1.5 lacs/mcl) decreased from 23 (57.5%) to 13 (32.5%) ($p=0.009$).

Table 4 reveals that there were considerable changes in bio-chemical profile of cases during the RNB intervention. Uraemia decreased from 6 cases (15%) to 3 cases (7.5%), elevated LDH levels decreased from 34 cases (85%) to 22 cases (55%), serum AST level decreased from 18 cases (45%) to 14 cases (35%), elevated CPK levels decreased from 9 cases (22.5%) to 6 cases (15%) and CRP positive cases 21 (52.5%) became negative on day 10 of the intervention.

Statistically significant association was observed only for changes in proportion of cases with elevated LDH values and CRP positive from day 1 to day 10 of RNB intervention ($p<0.001$).

Table 2: Effect of RNB on various clinical symptoms during the course of intervention on the basis of severity of illness (COVID-19).

S. no.	Presence of symptom	Day of intervention	Cases with mild illness n (%)	Cases with moderate illness n (%)	Cases with severe illness n (%)	Total cases Symptom present n (%)	Total cases Symptom absent n (%)	Cochran's Q test P value
1	Fever	Day 1	16 (40.0)	4 (10.0)	3 (7.5)	23 (57.5)	17 (42.5)	$\chi^2=35.58$ $P<0.001$
		Day 5	0 (0.0)	3 (7.5)	3 (7.5)	6 (15.0)	34 (85.0)	
		Day 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	40 (100.0)	
		Median 5 days and range 4 to 7 days						
2	Cough	Day 1	22 (55.0)	5 (12.5)	3 (7.5)	30 (75.0)	10 (25.0)	$\chi^2=47.38$ $P<0.001$
		Day 5	1 (2.5)	4 (10.0)	3 (7.5)	8 (20.0)	32 (80.0)	
		Day 10	0 (0.0)	0 (0.0)	1 (2.5)	1 (2.5)	39 (97.5)	
		Median 5 days and range 2 to 11 days						
3	Breathlessness	Day 1	0 (0.0)	6 (15.0)	3 (7.5)	9 (22.5)	31 (77.5)	$\chi^2=12.25$ $P=0.002$
		Day 5	0 (0.0)	3 (7.5)	3 (7.5)	6 (15.0)	34 (85.0)	
		Day 10	0 (0.0)	0 (0.0)	1 (2.5)	1 (2.5)	39 (97.5)	
		Median 7 days and range 3 to 11 days						
4	Sore throat	Day 1	12 (30.0)	3 (7.5)	3 (7.5)	18 (45.0)	22 (55.0)	$\chi^2=24.0$ $P<0.001$
		Day 5	1 (2.5)	3 (7.5)	2 (5.0)	6 (15.0)	34 (85.0)	
		Day 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	40 (100.0)	
		Median 5 days and range 3 to 11 days						
5	Fatigue	Day 1	14 (35.0)	3 (7.5)	2 (5.0)	19 (47.5)	21 (52.5)	$\chi^2=29.78$ $P<0.001$
		Day 5	1 (2.5)	3 (7.5)	1 (2.5)	5 (12.5)	35 (87.5)	
		Day 10	0 (0.0)	0 (0.0)	1 (2.5)	1 (2.5)	39 (97.5)	
		Median 5 days and range 3 to 11 days						
6	Myalgia	Day 1	7 (17.5)	3 (7.5)	3 (7.5)	13 (32.5)	27 (67.5)	$\chi^2=19.54$ $P<0.001$
		Day 5	0 (0.0)	3 (7.7)	3 (7.5)	6 (15.0)	34 (85.0)	
		Day 10	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	40 (100.0)	
		Median 5 days and range 2 to 9 days						

Table 3: Effect of RNB on haematological and microbiological profile of the study participants during course of intervention.

S. no.	Variable name	Sub-groups	Day 1 of intervention n (%)	Day 5 of intervention n (%)	Day 10 of intervention n (%)	Cochran's Q test P value
1	Anaemia status	Normal (male Hb ≥ 13 g/dl; non-pregnant female ≥ 12 g/dl)	15 (37.5)	16 (40.0)	19 (47.5)	$\chi^2=2.89$ $P=0.236$
		Anaemia (male Hb <13 g/dl; non-pregnant female <12 g/dl)	25 (62.5)	24 (60.0)	21 (52.5)	
2		Normal (4000-11000 mcl)	36 (90.0)	39 (97.5)	36 (90.0)	$\chi^2=3.00$

Continued.

S. no.	Variable name	Sub-groups	Day 1 of intervention n (%)	Day 5 of intervention n (%)	Day 10 of intervention n (%)	Cochran's Q test P value
	Total leukocyte count status	Leucocytosis (>11000 mcl)	4 (10.0)	1 (2.5)	4 (10.0)	P<0.223
3	Neutrophil-lymphocyte ratio (NLR)	Normal (<2.93)	22 (55.0)	25 (62.5)	29 (72.5)	$\chi^2=4.35$ P<0.113
		Abnormal (≥ 2.93)	18 (45.0)	15 (37.5)	11 (27.5)	
4	Thrombocytes status	Thrombocytopenia (<1.5 lac mcl)	23 (57.5)	19 (47.5)	13 (32.5)	$\chi^2=9.5$ P=0.009
		Normal (1.5 to 4.0 lac mcl)	17 (42.5)	21 (52.5)	27 (67.5)	
5	Naso-pharyngeal and oro-pharyngeal RT-PCR status	Positive	40 (100.0)	10 (25.0)	4 (10.0)*	$\chi^2=55.8$ P<0.001
		Negative	0 (0.0)	30 (75.0)	36 (90.0)	

Table 4: Effect of RNB intervention on bio-chemical profile of the study participants.

S. no.	Variable name	Sub-groups	Day 1 of intervention n (%)	Day 5 of intervention n (%)	Day 10 of intervention n (%)	Cochran's Q test P value
1	Serum urea	Normal level (10-45 mg/dl)	34 (85.0)	36 (90.0)	37 (92.5)	$\chi^2=1.56$ P=0.459
		Higher level (>45 mg/dl)	6 (15.0)	4 (10.0)	3 (7.5)	
2	Serum creatinine	Normal range (0.5-1.5 mg/dl)	38 (95.0)	39 (97.5)	39 (97.5)	$\chi^2=3.0$ P=0.223
		Higher creatinine level (>1.5 mg/dl)	2 (5.0)	1 (2.5)	1 (2.5)	
3	LDH status	Normal (<220 IU/l)	6 (15.0)	8 (20.0)	18 (45.0)	$\chi^2=19.08$ P<0.001
		Abnormal (≥ 220 IU/l)	34 (85.0)	32 (80.0)	22 (55.0)	
4	AST (SGOT) level	Normal (0-40 IU/l)	22 (55.0)	23 (57.5)	26 (65.0)	$\chi^2=2.6$ P=0.273
		Abnormal (>40 IU/l)	18 (45.0)	17 (42.5)	14 (35.0)	
5	ALT (SGPT) level	Normal (0-40 IU/l)	14 (35.0)	14 (35.0)	15 (37.5)	$\chi^2=0.14$ P=0.93
		Abnormal (>40 IU/l)	26 (65.0)	26 (65.0)	25 (62.5)	
6	C-reactive protein status	Positive	21 (52.5)	8 (20.0)	0 (0.0)	$\chi^2=32.1$ P<0.001
		Negative	19 (47.5)	32 (80.0)	40 (100.0)	
7	Creatine phosphokinase NAC status	Normal (<130 IU/l)	31 (77.5)	31 (77.5)	34 (85.0)	$\chi^2=2.57$ P=0.276
		Abnormal (≥ 130 IU/l)	9 (22.5)	9 (22.5)	6 (15.0)	

Table 5: Distribution of study cases on the basis of radiological findings (N=40).

Sub-groups	n (%)
Radiological status according to British society of thoracic imaging (BSTI)	
Normal	28 (70)
Non-COVID-19	2 (5)
Classic/probable COVID-19	4 (10)
Indeterminate for COVID-19	6 (15)
Lung involvement in classic/indeterminate COVID-19 cases (N=10)*	
Unilateral lung involvement	4 (40)
Bilateral lung involvement	6 (60)
Diffuse lung involvement	2 (20)
Peripheral lung involvement	8 (80)
Middle and lower zone lung involvement	10 (100)
Middle zone lung involvement only	0 (0.0)

*Multiple findings in cases

Radiological status according to British society of thoracic imaging (BSTI) classification revealed that 10 (25%) of them had radiological features in chest x-rays suggestive of COVID-19 and multiple lobe involvement was common (Table 5).

DISCUSSION

The mean \pm SD age of study subjects was 43.5 \pm 14.7 years (range from minimum 22 to maximum 80 years) and majority of the cases were male 31 (77.5%). Various studies too have reported that age is not a barrier to acquire the disease.⁶ The study revealed that 31 (77.5%) of the COVID-19 cases were having mild, 6 (15%) moderate and 3 (7.5%) having severe form of illness. Ten cases (25%) had co-morbidities and diabetes was the most common comorbidity.

In this study, all possible parameters, namely, clinical, hematological, microbiological, biochemical and radiological were analyzed and assessed in mild, moderate

and severe illness groups. Fever, cough, breathlessness, sore throat, fatigue and myalgia were the main presenting symptoms observed in cases enrolled for the study. Although a speedy recovery in all the clinical parameters were observed, but, overall symptomatic improvement was different when viewed in context to the grading of illness according to severity. In mild illness group, all the clinical symptoms subsided by day five of RNB intervention while in the moderate group, all symptoms subsided by day 7 to 8 days and in severe group, it took longer than 10 days. The association between day of evaluation from start of intervention and absence of clinical symptom was found to be statistically significant ($p < 0.001$, $p < 0.001$, $p = 0.03$, $p < 0.001$, $p < 0.001$ and $p < 0.001$) respectively. Rapid improvement of symptoms namely fever, cough and sore throat after RNB therapy clearly proves its immuno-modulatory, analgesic and anti-inflammatory effect. These effects may be attributable to Sulphur (gandhak) and the highly purified form of mercury (paara).⁷ Other researchers have also reported their significant analgesic and anti-inflammatory efficacy.⁸⁻¹⁰

Carum coptium (azwain) stimulates beta-2 receptors and blocks histamine (H_1) receptors in therapeutic doses and thereby relaxes the bronchial smooth muscles responsible for broncho-dilatory effect and pimentine (found in black pepper) acts as mucolytic agent.¹¹⁻¹³ Thus, both of these constituents help in reducing the replication of viruses in the upper respiratory tract mucosa.^{14,15} Significant improvement in the cough and breathlessness in cases of the present study may be due to cumulative effect of these ingredients of RNB, thereby, justifying the inclusion of gandhak, azwain and black pepper in RNB preparation.

Wilkerson et al reported silent hypoxia as a harbinger of clinical deterioration in the COVID-19 cases.¹⁶ None of the patient in the present study succumbed to silent hypoxia. All three cases of severe illness group had SpO_2 less than 90% on room air during hospitalization. But all these cases were discharged uneventfully. An important ingredient of RNB, hartal bhasma, affects allergen induced hyperresponsiveness of airways thereby improving airflow, ventilation perfusion and presumably prevented silent hypoxia in cases.¹⁷

Studies have documented that the hemoglobin value is significantly lower in COVID-19 cases with severe disease than those in milder forms.¹⁸⁻²⁰ The haemoglobin levels of 62.5% COVID-19 positive cases in the present study were found below their normal levels which presumably and mainly is due to nutritional deficiencies highly and quite prevalent in Indian population.

Initially considered primarily a respiratory illness, rapidly accumulating data suggests that COVID-19 results in a unique, profoundly prothrombotic milieu leading to both arterial and venous thrombosis. A severe inflammatory response, originating in the alveoli, triggers a dysfunctional cascade of inflammatory thrombosis in the pulmonary vasculature, leading to a state of local

coagulopathy.²¹ As per Ayurveda principles, kharpar, which is an ingredient of RNB, has antiplatelets effect and causes haemodilution to protect disseminated intravascular coagulopathy (DIC). The present study also depicted that there is a progressive increase in hemoglobin among 4 (10%) cases and thrombocytopenia decreased from 23 cases (57.5%) on day one of intervention to 13 cases (32.5%) on day 10 ($p = 0.009$) while other studies have reported that platelet counts were reduced only in 5.0 to 8.0% of cases.²²⁻²⁴ Better improvement in haematological profile of cases signifies the integrated response of the various allo-vedic constituents of RNB.

NLR is a novel marker of systemic inflammatory response which can also help to predict clinical severity in patients with COVID-19.²⁵ Normal ($NLR < 2.93$) increased from 22 cases (55%) to 29 cases (72.5%) which is a marker of improvement of COVID-19 illness. In the present study, there was lymphocytopenia among 35% of cases. Similar findings were seen in a research that found leukopenia, lymphopenia, raised aspartate aminotransferase in COVID-19 positive cases.²⁶ Some studies done in China, showed that 63.0%, 35.0%, 42.0% and 55.0% of cases had a decrease in lymphocytes respectively.^{19,22-24}

Viral shedding among study cases was assessed on the basis of conversion of throat and nasopharyngeal samples by RT-PCR from positive to negative. Viral shedding varies irrespective of disease severity. It was observed that 30 cases (75.0%) became negative for SARS-CoV-2 after day 5 while 4 cases (10.0%) remained RT-PCR positive on day 10 ($p < 0.001$). RNB intervention was given continuously to these cases till 12 days and subsequently all the study cases turned out to be negative on day 12. A systemic review concluded that length of hospital-stay ranged from 4 to 53 days within China and 4 to 21 days outside of China.²⁷ A retrospective cohort study conducted in Wuhan, China among cases with COVID-19 showed viral shedding range between 8 and 37 days. The median duration of viral shedding was 20 days in survivors, but continued till death in fatal cases.²⁸ But, in the present study, as the clinical and microbiological (RT-PCR-negative) status turned out to be negative within 5 days of RNB intervention in majority of COVID cases, this rapid conversion of cases as RT-PCR negative is clearly indicative of antiviral activity of silver nanoparticles in silver bhasm which is an ingredient of RNB. Role of silver bhasm in inhibition of H1N1 influenza viral agglutination and reduction of viral induced apoptosis have also been reported in previous researches.²⁹ An article published in 2019 reported a remarkable antiviral activity against HSV-1, HAV-10, and Cox-B4 virus of green synthesized silver nano-particles (SNPs).³⁰ Another researcher reported that oedema decreased with production of cytokines, induced by ultraviolet B rays (UVB) indicating anti-inflammatory activity of SNPs.⁸ Similarly zinc containing compound (kharpar) and *Clamina perpeta* were reported to inhibit the activity of SARS-CoV polymerase by decreasing its replication.³¹ Hence, it is interpreted that public health

burden can be ameliorated by the use of RNB in affected sections of the community.

In various studies, LDH has been identified as predictor for recognition of lung injury and severe COVID-19 cases. LDH is not only a metabolic but also an immune-surveillance prognostic biomarker and its elevation is harbinger of negative outcome in immunosuppressive cases. Increased levels of LDH have been reported among 73%, 76%, 92%, 69% of cases respectively in various studies of China).^{19,22,24,32} A multicentric nested case control study concluded that high LDH level (≥ 220 IU/l) is independent risk factor for exacerbation in mild COVID-19 cases and about the 8-30% of cases would eventually develop severe illness.³³ Present study also observed that LDH was high in majority 34 (85%) of cases and remained high in 28 cases (70%) till day 10 of intervention. The interesting observation was that, among them, no adverse reactions in vitals were noted and none converted to the severe illness. Probably, it may be hypothesized that RNB helped in preventing the deterioration of cases in spite of increase in LDH levels. As LDH is an overall marker of various tissue destruction in the body, hence, hartal bhasma as RNB constituent was beneficial due to decreased activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), a protein complex that controls transcription of DNA, cytokine production and cell survival.³⁴ Although, this aspect needs to be studied further.

Plasma CRP level is correlated with severity of the COVID-19 and used as a prognostic marker.³⁵ In the present study, CRP was positive in 21 cases (52.5%) at the time of admission which gradually declined to 8 cases (20%) on day 5 and all cases were negative on day 10 of RNB intervention. This effect signifies the immune-modulatory and anti-inflammatory properties of various ingredients of RNB.

Portable chest x-ray is the most commonly performed radiological investigation in terms of feasibility and cost effectiveness even in developed nations. In the present study, radiological findings were described according to British society of thoracic imaging guidelines.³⁶ According to it, the COVID-19 cases were segregated into normal cases 28 (70%), classic COVID-19 pneumonia cases 4 (10%), indeterminate cases 6 (15%) and non-COVID-19 cases as 2 (5%) and these findings were further distributed as unilateral versus bilateral, diffuse versus peripheral and lower and middle zone versus only middle zone on the basis of pattern of lung involvement. Classic COVID-19 pneumonia, as described in international studies, have bilateral, peripheral ground glass opacities and consolidation. Indeterminant group included, radiological characterization of COVID-19, keeping in view, presence of tuberculosis, allergic chest infections, hypersensitive pneumonitis that does not fit classic or non-COVID description. Non COVID-19 chest x-ray finding included, isolated pneumothorax, lobar pneumonia, pleural effusion, pulmonary edema and other preexisting chest X-ray

finding. Resolution of more than 50% in chest x-ray finding were observed after 10 to 12 days of RNB intervention. Since, the cases were discharged usually till day 14, as per national discharge policy guidelines, it was not possible to follow-up the patient to observe and report the complete resolution of radiological finding, which usually occurs by 3-4 weeks. Findings of consolidation in COVID-19 cases have also been reported by Salehi et al.³⁷

In Ayurveda, sulphur (gandhak) and *Artemisia nilagirica* (nag daminti) have been used for years considering its antibacterial, antifungal and anti-viral properties for many diseases. A study conducted on a sulphur compound for allergic rhinitis (methyl-sulfonylmethane) showed a statistically significant reduction in symptoms of upper respiratory tract from baseline ($p < 0.01$ respectively) on 7th day, whereas lower respiratory tract symptoms were improved significantly from baseline by third week ($p < 0.001$).³⁸

This is also an invaluable opportunity for demonstrating the efficacy of allo-vedic, a new system of medicine. Further randomized controlled trials (RCT) should be planned to test the hypothesis regarding the safety and effectiveness of the novel formulation (RNB).

CONCLUSION

The findings of the present study illustrates that there is a wide scope to explore the variety of pertinent medicines present in Ayurvedic pharmacopoeia which can be used more rationally to suit every stage of the disease based on modern scientific researches. Also, it is evident from the present study that allo-vedic drug RNB produces considerable beneficial effects on cases of COVID-19. Immuno-modulatory, anti-inflammatory and analgesic effect evident by quick symptomatic relief in fever, sore throat and fatigue and myalgia. Quick improvement of symptoms related to upper and lower respiratory tract namely cough and breathlessness imparted by mucolytic and broncho-dilatory action of its ingredients. Anti-viral properties apparent from the early symptomatic improvement as well as early negative naso-pharyngeal and oro-pharyngeal RT-PCR results. Hematopoietic effects namely improvement in haemoglobin status, better NLR and reduction in thrombocytopenia indicates that allo-vedic RNB have favorable outcome on all three-cell lineage, that is, RBC, WBC and platelets. Moreover, none of the patients reported DIC thereby providing evidence of inhibition of haemo-coagulation.

Thus, immunomodulatory, anti-inflammatory, anti-viral, broncho-dilatory, mucolytic, haemo-booster and anti-coagulatory properties of various ingredients makes RNB an ideal drug/weapon to fight against COVID-19 illnesses. This should encourage the healthcare policy makers to quickly use allo-vedic drug RNB to bring COVID-19 pandemic under control in India, as has been demonstrated in China with traditional Chinese medicine (TCM).

ACKNOWLEDGEMENTS

Authors would like to thank Yogi Nirwan Dev for his expertise in recognizing, isolating, processing and formulation of dosage of the allo-vedic preparation, Raj Nirwan Bati.

Funding: The study was funded by the Uttar Pradesh University of Medical Sciences, India

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Girija PLT, Sivan N. Ayurvedic treatment of COVID-19/SARS-CoV-2: A case report. *J Ayurveda Integr Med.* 2020;975-9476(20):30042-5.
- Shanghai Institute of Materia Medica website, Chinese. Academy of Sciences. A joint research team between the Shanghai Institute of Materia Medica and the University of Science and Technology of the Chinese Academy of Sciences has discovered a group of old and traditional Chinese medicines that may have a therapeutic effect on new pneumonia. Available at: http://www.simm.ac.cn/xwzx/kydt/202001/t20200125_5494417.html. Accessed on 27 May 2020.
- Kumar Y, Singh H. In Silico identification and docking-based drug repurposing against the main protease of SARS-CoV-2, causative agent of COVID-19. 2020;13(9):1210-23.
- Central Council for Research in Ayurveda and Siddha, 2009, Management of Chikungunya Through Ayurveda And Siddha. New Delhi. Available at: http://www.ccras.nic.in/sites/default/files/22092016_management%20of%20chikungunya%20through%20ayurveda%20and%20siddha-a%20technical%20report.pdf. Accessed on 27 May 2020.
- Kumar R, Yadav R, Rawat R, Bajpai PK, Sharma IK, Kumar S, et al. Raj Nirvan Bati (A Novel Ayurvedic Preparation) in RT-PCR positive COVID-19 Cases: An Interventional Study. *Int J Med Sci Curr Res.* 2020;3(3):430-40.
- Qifang B, Yongsheng W, Shujiang M, Chenfei Y, Xuan Z, Zhen Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis.* 2020;20(8):911-9.
- Yamamoto K, Hasobe M, Saneyoshi M. Inhibitory effect of sulphur-containing purine nucleoside analogues on replication of RNA viruses: selective antiviral activity against influenza viruses. *Acta Virol.* 1988;32(5):386-92.
- David L, Moldovan B, Vulcu A, Olenic L, Perde-Schrepler M, Fischer-Fodor E, et al. Green synthesis, characterization and anti-inflammatory activity of silver nanoparticles using European black elderberry fruits extract. *Colloids Surf B Biointerfaces.* 2014;122:767-77.
- Jayabharathi M, Musthafa M. Analgesic and anti-inflammatory efficacy on siddha drug rasa chendooram. *Semantic Scholar.* 2014;74036416.
- Ilbäck NG, Wesslén L, Fohlman J, Friman G. Effects of methyl mercury on cytokines, inflammation and virus clearance in a common infection (Coxsackie B3 myocarditis). *Toxicol Lett.* 1996;89(1):19-28.
- Boskabady M, Rakhshandah H, Moetamedshariati V. Bronchodilatory and anticholinergic effects of Carum copticum on isolated guinea pig tracheal chains. *Med J Islam Repub Iran.* 1998;11(4):329-34.
- Boskabady MH, Shaikhi J. Inhibitory effect of Carum copticum on histamine (H1) receptors of isolated guinea-pig tracheal chains. *J Ethnopharmacol.* 2000;69(3):217-27.
- Tousi MAM. Stimulatory Effect of Caruim Coptlcum on Beta-2 adrenoceptors of isolated guinea pig tracheal chains. *Med J Islam Repub Iran.* 2000;13(4):273-8.
- Spices for Lung Diseases. The national medical journal of India. Available at: <http://archive.nmji.in/approval/archive/Volume-3/issue-2/editorial1s-2.pdf>. Accessed on 29 May 2020.
- Basic elements in a system of chronic health care, Comparison of British, Canadian, Australian and American methodology - 2nd edition. Washington: U.S. Government Printing Office. 1966;316.
- Wilkerson RG, Adler JD, Shah NG, Brown R. Silent hypoxia: A harbinger of clinical deterioration in patients with COVID-19. *Am J Emerg Med.* 2020;159011-3.
- Zhou LF, Zhu Y, Cui XF, Xie WP, Hu AH, Yin KS. Arsenic trioxide, a potent inhibitor of NF- κ B, abrogates allergen-induced airway hyperresponsiveness and inflammation. *Respir Res.* 2006;7(1).
- Lippi G, Mattiuzzi C. Hemoglobin value may be decreased in patients with severe coronavirus disease 2019. *Hematol Transfus Cell Ther.* 2020;42(2):116-7.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *The Lancet.* 2020;395(10223):507-13.
- Kumar R, Yadav R, Rawat R, Bajpai PK, Sharma IK, Kumar S, et al. Role of Raj Nirvan Bati in treatment of COVID-19 RT-PCR Positive Cases. *Int J Sci Res Methodol.* 2020;15(4):1-9.
- Abou-Ismaïla MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. *Thrombosis Research.* 2020;194:101-15.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet.* 2020;395(10223):497-506.
- Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected

- with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ.* 2020;368.
24. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci.* 2020;63(3):364-74.
 25. Feng X, Li S, Sun Q, Zhu J, Chen B, Xiong M, Cao G. Immune-Inflammatory Parameters in COVID-19 Cases: A Systematic Review and Meta-Analysis. *Front Med.* 2020;7:301.
 26. Lake MA. What we know so far: COVID-19 current clinical knowledge and research. *Clin Med.* 2020;20(2):124-7.
 27. Eleanor MR, Nightingale ES, Jafari Y, Waterlow NR, Samuel C, et al. COVID-19 length of hospital stay: A systematic review and data synthesis. *BMC Med.* 2020;18:270.
 28. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *The Lancet.* 2020;395:1054-62.
 29. Xiang D, Chen Q, Pang L, Zheng C. Inhibitory effects of silver nanoparticles on H1N1 influenza A virus in vitro. *J Virol Methods.* 2011;178(1-2):137-42.
 30. Motamed MP, Tabatabaeian N, Sid MT. In vitro antiviral effect of "Nanosilver" on influenza virus. *DARU J Pharm Sci.* 2009;17(2).
 31. te Velthuis AJW, van den Worm SHE, Sims AC, Baric RS, Snijder EJ, van Hemert MJ. Zn²⁺ inhibits coronavirus and arterivirus RNA Polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. *PLoS Pathog.* 2020;6(11):e1001176.
 32. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Zhonghua Jie He He Hu Xi Za Zhi.* 2020;43(0):e005.
 33. Shi J, Li Y, Zhou X, Zhang Q, Ye X, Wu Z. Lactate dehydrogenase and susceptibility to deterioration of mild COVID-19 patients: A multicenter nested case-control study. *BMC Med.* 2020;18:168.
 34. Zhou LF, Zhu Y, Cui XF, Xie WP, Hu AH, Yin KS. Arsenic trioxide, a potent inhibitor of NF- κ B, abrogates allergen-induced airway hyperresponsiveness and inflammation. *Respir Res.* 2006;7(1).
 35. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. *Ann Clin Microbiol Antimicrob.* 2020;19.
 36. Rodrigues JC, Hare SS, Edey A, Devaraj A, Jacob J, Johnstone A, et al. An update on COVID-19 for the radiologist-A British society of thoracic imaging statement. *Clin Radiol.* 2020;75(5):323-5.
 37. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. *Am J Roentgenol.* 2020;1-7.
 38. Barrager E, Veltmann J, Schauss A, Schiller R. A multicentered, open-label trial on the safety and efficacy of methylsulfonylmethane in the treatment of seasonal allergic rhinitis. *J Alternat Complement Med.* 2002;8(2):167-73.

Cite this article as: Kumar R, Yadav R, Rawat R, Singh NP, Sharma IK, Yadav P. Evaluating effects of allo-vedic preparation Raj Nirwan Bati on symptomatic cases of COVID-19 at a tertiary level health care facility in rural setting of northern India. *Int J Res Med Sci* 2021;9:3289-97.