The efficacy of an Ayurvedic polyherbal formulation in the symptomatic management of mild COVID-19 cases: A double blind, randomized controlled trial

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Abstract

Purpose

The COVID-19 pandemic, caused by the SARS-CoV-2 virus has infected millions of people globally, overwhelming the pharmaceutical industry and health care systems. The resulting crisis has highlighted the need for modern and traditional medicine systems to work together to find effective solutions quickly. Modern systems of medicine are primarily oriented towards symptomatic treatment, whereas the traditional systems of medicine such as Ayurveda emphasize prevention as well as treatment.

Patients and methods

NF2 is polyherbal Ayurvedic formulation consisting of 19 ingredients from 13 herbs. 50 patients with confirmed symptomatic or asymptomatic case of COVID-19, reporting to the study site were invited to participate in a double blinded, randomized placebo-controlled clinical trial. The study duration was around 3 months, and the intervention period for an individual patient was 10 days.

Results

Significant improvements were observed in the NF2 arm in comparison to the placebo arm. On Day 5, the population in the NF2 arm showed a complete recovery from sputum formation, sore throat, headache and fever. By Day 10, 90-100% of the population in the NF2 arm showed a complete recovery from all symptoms, unlike the control arm.

Conclusion

NF2 facilitated a complete recovery from all clinical features of COVID-19 faster, when compared to the control. No side effects were observed during the entire study duration.

Introduction

The COVID-19 pandemic caused by the SARS-CoV-2 virus has infected millions of people around the globe in over 200 countries. Thousands have been hospitalized and even more have required health care support.¹ The high rate of transmission, quick mutations and rapidly evolving variants of the virus have hindered the discovery of a therapeutic cure.²⁻³ The modern pharmaceutical and health care system are overwhelmed.

The pandemic has highlighted the need for modern and traditional systems of medicine to support each other. The current system of medicine is primarily oriented towards symptomatic treatment of disease, whereas several traditional systems of medicine like Ayurveda advocate prevention, as well as treatment. Ayurveda is a traditional Indian system of medicine, practiced in India for over 5000 years. Compared to conventional pharmaceuticals, bioactive natural compounds found in Ayurvedic medicines, tend to have good biocompatibility and bioavailability, less toxicity and have ample phytoconstituents such as phenols, steroids and flavonoid molecules.⁴ Ayurvedic treatments are being studied extensively for the cure of COVID-19. An earlier study explored the immunomodulatory and anti SARS-CoV-2 effects of Ashwagandha (*Withania somnifera*), Guduchi (*Tinospora cordifolia*) and Shatavari (*Asparagus racemosus*) using network pharmacology and docking.⁵ A retrospective observational study to evaluate the impact of Ayurveda treatment on COVID-19 observed that Ayurveda treatment improves clinical recovery.⁶ This study investigates the efficacy of a polyherbal Ayurvedic formulation called NF2 in the management of COVID-19. NF2 contains 19 ingredients from 13 Ayurvedic herbs including Ashwagandha (*Withania somnifera*), Vasaka

(*Adhatoda vasica*), Guduchi (*Tinospora cordifolia*), and Yashtimadhu or Licorice (*Glycyrrhiza glabra*) etc. A robust immune system plays an important role in protecting against communicable diseases, such as COVID-19.⁷ Several constituents of NF2 have immunomodulatory, antiviral, anti-inflammatory, and antioxidant properties. Earlier studies on individual constituents have investigated each of them for their properties separately. Ashwagandha alone has about 69 (39 preclinical and 30 clinical) studies related to its safety and efficacy.⁸ Ashwagandha (*Withania somnifera*) is a prime medicinal plant of indigenous medicine. It is an immune booster and has hepatoprotective, anti-inflammatory, antioxidant and immunomodulatory properties.⁹ A molecular docking study on Ashwagandha (*Withania somnifera*), Guduchi/ Giloy (*Tinospora cordifolia*) and Tulsi (*Ocimum sanctum*) (all three are present in NOQ 19) showed a promising effect against COVID-19.¹⁰ Another constituent of NF2, Yashtimadhu or Licorice (*Glycyrrhiza glabra*) is potent in treating respiratory tract infections, dry cough and hoarseness. It is reported to have antiviral effects as well.¹¹ A molecular docking study revealed that various phytochemicals found in Yashtimadhu (*Glycyrrhiza glabra*) have significant binding affinity with SARS-CoV-2 proteins.^{12–13} An earlier study showed the antimicrobial, antioxidant and cytotoxic properties of the alkaloids from the herb Vasaka (*Adhatoda vasica*). Vasaka (*Adhatoda vasica*) is used to treat chronic fever, cough, and asthma because of its antitussive activity.¹⁴ In acute stage of bronchitis, Vasaka gives unfailing relief, especially when the sputum is thick and sticky.¹⁵ Its antispasmodic and expectorant properties make it very effective in treating respiratory conditions.¹⁶ The extracts and compounds isolated from Bhumihamla (*Phyllanthus fraternus*), also present in NF2, and show a wide spectrum of pharmacological activities including antiviral, antibacterial, antispasmodic, anti-inflammatory, antioxidant, hepatoprotective and diuretic properties.¹⁷ Bhunimba (*Andrographis paniculata*), another ingredient of NF2, commonly known as Kalamegha, is reported to have hepatoprotective, antiulcer, anti-inflammatory and antipyretic properties. Clinically, it has shown significant result in viral hepatitis, common cold, vitiligo and upper respiratory tract infections.¹⁸ It is traditionally used for the treatment of common cold, diarrhoea, fever secondary to infection, and as a health tonic for the liver and heart.¹⁹ Turmeric (*Curcuma longa*), another constituent of NF2, has been shown to benefit inflammatory conditions and reduce pain.²⁰ Tulsi or holy basil (*Ocimum sanctum*), another constituent of NF2, is one of the most extensively used medicine in Ayurveda. It is considered a potent adaptogen that promotes wellbeing and resilience. It is antimicrobial, antioxidant, anti-inflammatory, neuro-protective, cardio-protective, analgesic, anti-pyretic and immunomodulatory in nature.²¹ An *in vitro* study conducted on the efficacy and safety of NF2 showed a 100% antiviral efficacy of NF2 in Vero E6 cells.²² An *in vivo* study in Syrian golden hamsters demonstrated a greater than 78% reduction in viral load when treated with NF2.²³ Analysis of a pilot study on NF2 demonstrated that 74% of patients turned RT-PCR negative within 5 days of taking NF2. Additionally, 98% of the subjects turned RT-PCR negative on day 10 after taking NF2 along with standard care of treatment including Vitamin C, Zinc and antipyretic as needed. No participants reported adverse events. The objective of this clinical trial is to investigate the safety and efficacy of NF2, provided in addition to the standard therapy, for patients with mild COVID-19, by specifically measuring the symptomatic parameters.

Material And Methods

2.0 Study Design

The study was a double blind, randomized placebo-controlled clinical trial. The trial was conducted at Sri Sri college of Ayurvedic Science & Research Hospital, Sri Sri University, Cuttack, Odisha. The study was approved by the Institutional Ethics Committee, Sri Sri University (IEC Number- SSCASRH/IEC/001/21) and registered with CTRI No. CTRI/2021/08/036025. The duration of the study was from 1st to 25th September 2021. The participants were

recruited during the entire study period, as and when they reported to the hospital. The intervention period for an individual patient was 10 days.

2.1 Participants

All patients who reported to inpatient (IPD) and outpatient (OPD) sections of COVID Care Centre at Sri Sri College of Ayurvedic Science & Research Hospital, Sri Sri University, Cuttack, Odisha, were invited to participate in the trial. Each patient with a confirmed symptomatic or asymptomatic case of COVID-19 was informed about the purpose of the clinical trial. Informed consent was obtained from those who wished to enroll in the study. Participants were informed about the insurance details, and were made aware that they could withdraw from the study at any time. Their written informed consent was obtained via a study specific proforma prepared for this trial, which included demographic information and baseline study parameters. 50 RT-PCR positive COVID-19 patients were enrolled after receiving their written consent. A total of 6 Patients were excluded from the study due to noncompliance. 25 patients in the NF2 arm and 19 patients in the placebo arm completed the clinical trial. The trial had to be terminated due to non-availability of COVID-19 patients.

2.1.1. Inclusion Criteria

- a. Asymptomatic or symptomatic RT-PCR positive mild to moderate COVID-19 cases (without comorbidities) as per the GOI norms
- b. History of fever of >98.60F
- c. Cough
- d. Dyspnea (shortness of breath) or Tachypnea
- e. Patients of both genders between the ages of 18-77 years
- f. Indian Nationals
- g. Willingness to participate in the study with a written consent

2.1.2. Exclusion Criteria

- a. Not willing to give consent/ participate in the clinical trial
- b. Age less than 18 years or more than 75 years
- c. Patients with comorbidities such as uncontrolled hypertension, diabetes, thyroid disorder, Heart/ Lung/Liver/Renal disorder, moderate to severe anaemia / hematological disorders, Malignancy, Stroke: ischaemic stroke & intracerebral haemorrhage,
- d. Patients on immunosuppressive therapy
- e. Pregnant women or lactating mothers
- f. Any major surgery in the last six months or hospitalized for more than three days for any condition.

2.3 Intervention

Each patient was monitored for 10 days. Follow up assessments were conducted on day 5 and day 10. One nasal and one throat swab was obtained for RT-PCR on day 5 and 10 through an ICMR accredited laboratory. The patients were advised to inform the hospital staff immediately in case of any adverse events and/or aggravation of symptoms. Compliance with the treatment was assessed and subjects were counselled for dosage compliance in person.

2.3.1. NF2 preparation

NF2 also known as NOQ19. NF2 also is polyherbal formulation with 19 ingredients from 13 herbs. They are Ashwagandha (*Withania somnifera*) powder and extract, Bilwa (*Aegle marmelos*), Yashtimadhu (*Glycyrrhiza glabra*) powder and extract, Rasna (*Pluchea lanceolata*), Vasaka (*Adhatoda vasica*) powder and extract, Pippali (*Piper longum*), Haridra (*Curcuma longa*), Patha (*Cissampelos pareira*), Bhumiamla (*Phyllanthus fraternus*) powder and extract, Bhunimba (*Andrographis paniculata*) powder and extract, Saptaparna (*Alstonia scholaris*), Tulasi (*Ocimum sanctum*) and Guduci (*Tinospora cordifolia*) powder and extract. NF2 was procured from Sriveda Sattva Pvt Ltd, Bangalore (Sri Sri Tattva). The drug was licensed by Ministry of AYUSH, Govt. of India with the license number-AUS782. All the herbs which constituted NF2 were subjected to quality control. All the ingredients were blended with excipients followed by granulation, drying and compression. Once the tablet passed the QC tests, it was packed in bottles following standard procedure.

2.3.2. NF2 group

Participants enrolled in the NF2 arm were given the NF2 tablets. The dosage for NF2 arm was 2 tablets (500 mg each) thrice a day after food for 10 days.

2.3.3. Comparator Group

The placebo control group was provided the placebo tablets made of starch. They were packed in bottles identical to the NF2 bottles by Sri Sri Tattva. The dosage for placebo arm was also 2 tablets (500 mg each) thrice a day after food for 10 days.

2.3.4. Standard treatment

In addition to receiving NF2 or placebo, both groups received the standard treatment according to the government guidelines. The standard treatment included Azithromycin (500mg, once a day for 5 days) or Doxycycline (100mg, twice a day for 5 days), Levocetirizine (5mg once a day for 5 days), Vitamin C (10 days), Zinc (10 days) and Paracetamol (500mg, as required).

2.4 Outcomes

Clinical history was obtained from each participant enrolled in the study, followed by clinical examination and baseline investigations.

2.4.1. Primary Outcome

The primary outcome was the percentage of population turning RT-PCR negative by Day 5 and 10 in both study arms. One nasal and one throat swab was collected from each patient and subjected to the PCR analysis to identify the viral load in patients.

2.4.2. Secondary Outcomes

The secondary outcomes included the assessment of subjective parameters such as sore throat, cough, runny nose, shortness of breath, joint pain, fatigue, headache, loss of smell and loss of taste in both groups on Day 5 and Day 10 (Supplementary Table 1). The presence or absence of subjective outcomes was noted for each patient, in person, at each follow up time point, based on their baseline clinical history. Recovery or clinical improvement of patients was in par with the discharge policy provided by the Government of India.²⁴ Observations of adverse events or side effects were also included in the secondary outcome. The assessment form has been provided for reference at the end of the paper as a supplementary table 1.

2.5. Sample size calculation

Based on the previous studies done on similar drugs, the study sample size was calculated to be 50 in each arm.²⁵ But there was sharp decline in COVID cases at site so the enrollment had to close at 25 patients per arm.

2.6. Randomization and blinding

The study participants were allocated into different study arms with the help of a computer generated randomization code. The allocation was sequentially distributed. Since both NF2 and placebo were packaged in identical bottles, the participants were blinded to the respective intervention. The participants, data collector and the laboratory technician were blinded to the study group allocation.

2.7. Statistical analysis

The baseline characteristics of both study groups were reported as proportion/ mean (SD). Data analysis was conducted using the Intention To Treat (ITT) approach. The categorical variables were listed as number and percentage (%). The quantitative data was presented as the means $\pm$ SD. The data normality was checked using Kolmogorov-Smirnov test. In cases where the data was not normal, non-parametric tests were used. The quantitative variables, not normally distributed in nature, were analyzed using the Mann-Whitney Test (for two groups) and Independent t test was used for comparison of normally distributed data between two groups. Paired t test/Wilcoxon signed rank test was used for comparison across follow up. The variables which were qualitative in nature were compared and analyzed using Chi-Square test. If any cell had an expected value of less than 5, then Fisher's exact test was used. The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 2.0. For statistical significance, p value of less than 0.05 was considered statistically significant. (Fig 1)

Results

A total of 50 participants were enrolled in the study, 25 in each arm. Those who did not adhere to the protocol or could not comply were excluded from the data analysis. No significant difference was found in the age and gender distribution or co-morbidities between the two groups. The duration between the onset of symptoms, positive COVID-19 test and the enrollment in NF2 or control arm group was also similar. Both the groups were predominantly male. Table 1 lists the demographic characteristics of the study population.

Table 1
Demographic Characteristics of the study population.

Demographic characteristics	NF2 (n=25)	Placebo (n=19)	Total	p value
IPD (n)	25	19	44	NA
Age Range (yrs)	18-74	18-50	18-74	
Age (Mean $\pm$ SD)	38.96 $\pm$ 16.90	28.11 $\pm$ 9.28	34.27 $\pm$ 15.00	0.015*
Female (n %)	10 (40%)	7 (37%)	27 (61.4%)	1.00
Male (n %)	15 (60%)	12 (63%)	17 (39.4%)	
SPO2 (Mean $\pm$ SD)	97.56 $\pm$ 0.70	97.58 $\pm$ 0.69	97.57 $\pm$ 0.69	0.91
Temp (Mean $\pm$ SD)	98.51 $\pm$ 1.15	98.52 $\pm$ 1.15	98.54 $\pm$ 1.13	0.97
Pulse Rate per min. (Mean $\pm$ SD)	82.93 $\pm$ 5.16	83.11 $\pm$ 10.45	83.00 $\pm$ 7.68	0.93
Respiratory Rate per min. (Mean $\pm$ SD)	20.08 $\pm$ 1.26	19.11 $\pm$ 0.88	19.67 $\pm$ 1.21	0.006*
* <0.05 -significant				

(Table 1)

Table 1 shows no significant difference in the age and gender distribution between the two groups. The duration between the onset of symptoms, positive COVID-19 test and the enrollment in NF2 or placebo arm was also similar.

3.0 Primary Outcome - % population with RT-PCR Negative test

19 out of the 25 patients (76%) in the NF2 arm turned RT-PCR negative after 5 days of treatment (Table 2). By Day10 all patients in both arms were RT-PCR negative. (Table 2)

Table 2
Percentage of Population with RT-PCR negative test at Day 05

	NF2 (n=25)	Placebo (n=19)	Intergroup p value
Day 0	0 (0%)	0 (0%)	
Day 5	19 (76%)	0 (0%)	$<0.001^{**}$
Intragroup p value	$<0.001^{**}$	NA	
* $p<0.05$ -significant			
** $p<0.001$ -very significant			

Table 2 shows that NF2 arm had a 76% increase in patients who turned RT-PCR negative on Day 5, while the placebo arm showed no improvement. Patients in the NF2 arm showed an early and strong recovery from COVID-19.

3.1 Secondary Outcome - Symptomatic Recovery

The secondary outcomes included subjective parameter assessments of sore throat, cough, runny nose, shortness of breath, joint pain, fatigue, malaise, headache, loss of smell and loss of taste in both groups on Day 5 and Day 10.

(Table 3)

Table 3
Rate of symptom recovery at Day 5 and Day 10

Clinical features	NF2 n(%)			Placebo n(%)			Intergroup p value between the 2 arms		
	D-1	D-5	D-10	D-1	D-5	D-10	D-1	D-5	D-10
Fever (Afebrile)	16 (64%)	23 (100%)	23 (100%)	12 (63.2%)	18 (94.7%)	18 (100%)	<0.001**	0.45	1.00
Absence of Dry Cough	20 (80%)	21 (84%)	22 (100%)	13 (68.4%)	13 (68.4%)	17 (89.5%)	<0.001**	0.11	0.45
Absence of Hemoptysis	25 (100%)	23 (100%)	22 (100%)	19 (100%)	19 (100%)	19 (100%)	1.00	1.00	1.00
Absence of Sputum Formation	18 (72%)	23 (100%)	23 (100%)	13 (68.4%)	13 (68.4%)	15 (78.9%)	<0.001**	<0.001**	0.08
Absence of Sore Throat	14 (56%)	23 (100%)	22 (100%)	12 (63.2%)	12 (63.2%)	16 (84.2%)	0.09	<0.001**	0.19
Absent Runny nose	0 (0%)	18 (72%)	22 (100%)	1 (5.3%)	3 (15.8%)	13 (68.4%)	<0.001**	0.003**	0.013*
Absence of Shortness of breath	25 (100%)	23 (100%)	22 (100%)	19 (100%)	18 (100%)	18 (100%)	1.00	1.00	1.00
No Headache	6 (24%)	22 (100%)	21 (100%)	1 (5.3%)	4 (21.1%)	14 (73.7%)	0.084	<0.001**	0.037**
No Fatigue (can do normal work)	20 (80%)	22 (100%)	22 (100%)	17 (89.5%)	17 (89.5%)	18 (100%)	<0.001**	0.58	1
Absence of Joint Pain (No pain)	12 (48%)	16 (64%)	21 (100%)	5 (26.3%)	6 (31.6%)	6 (31.6%)	0.15	0.019**	<0.001* *
Absence of Anosmia (Normal Smell)	24 (48%)	16 (64%)	22 (100%)	9 (47.4%)	9 (47.4%)	10 (52.6%)	0.063	<0.001**	0
Absence of Aguesia (Normal Taste)	11 (44%)	16 (64%)	22 (100%)	10 (52.6%)	10 (52.6%)	9 (47%)	0.011*	<0.001**	<0.001* *
*<0.05-significant									
**<0.001-very significant									

Table 3 depicts the improvement in the symptomatic clinical features of COVID-19. There was a negligible difference in the severity of clinical features between the two groups on Day 1. On Day 5, the population in the NF2 arm showed a complete recovery from sputum formation, sore throat, headache and fever. By Day 10, 90-100% of the population in NF2 arm showed a complete recovery from all symptoms, unlike the control arm. No adverse events or side effects were observed during the study duration in the NF2 arm.

Discussion

COVID-19 is a highly communicable disease that can cause severe pneumonia and acute respiratory distress syndrome.²⁶ The results of the study demonstrate a significantly faster recovery from clinical symptoms of COVID-19 in the NF2 arm, both for the time taken to experience relief from clinical symptoms and the time taken for RT-PCR to turn negative from positive. The patients in NF2 arm recovered faster than the placebo arm, as depicted in Table 3. 76% of the patients in NF2 arm turned RT-PCR negative by day 5. The results of this clinical study are supported by earlier studies on NF2. An *in vitro* study conducted on the efficacy and safety of NF2 showed 100% antiviral efficacy of NF2 in Vero E6 cells.²² An *in vivo* study in the Syrian golden hamsters demonstrated a greater than 78% reduction in viral load when treated with NF2.²³ One of our earlier pilot feasibility study demonstrated that 74% of patients turned RT-PCR negative within 5 days of taking NF2, and 98% of the subjects turned RT-PCR negative on day 10 after taking NF2, along with standard care of treatment of Vitamin C, Zinc and antipyretic (if necessary). None of the participants reported any adverse events. This study investigated the impact of NF2 on the common clinical features of COVID-19 and found significant improvement in almost all of them, compared to the placebo arm. One of the common syndromes associated with COVID-19 are its post COVID complications. Studies quote the persistent COVID-19 complications until almost 24 weeks among SARS-CoV-2 infected population. These symptoms vary depending on the severity of illness.²⁷⁻²⁸ Our study demonstrated a speedy recovery of symptoms like fatigue also among COVID-19 infected patients. Patients report acute respiratory problems like chronic cough, fibrotic lung disease, bronchiectasis and pulmonary vascular disease. These long term respiratory distress syndrome decrease the lung capacity and quality of life.²⁹ Fast recovery with absence of shortness in breath, as discovered in the NF2 group can help patients cope the distress and improve patients' lung capacity. Previous pre-clinical studies on Vasaka (*Adhatoda vasica*) demonstrate an anti-hypoxic effect of the drug on the mice model.³⁰ Guduchi (*Tinospora cordifolia*) has been previously used in the management of Bronchial asthma (Tamaka Swasha).³¹ Presence of the above mentioned herbs in NF2 may be a contributor of associated symptom recovery and absence of breathlessness in patients. Presence of Yashtimadhu and Ashwangandha, as demonstrated by many *in-silico* studies may contribute to inhibition of viral protein attachment to lung ACE-2 cell receptors, that may reduce the viral load.³²⁻³³ Ashwangandha a popular ayurvedic drug has been investigated for its role in decreasing fatigue as also noted in patients from NF2 arm.³⁴ The study has certain limitations. The study period saw a decline in the number of COVID-19 patients; hence the sample size was small. Another limitation was the non-inclusion of patients with comorbidities, as well as absence of blood biomarker assessment. Similar trials can be conducted on a larger population, including patients with comorbidities, to confirm the results of the present study. Most of the Ayurvedic studies are done *in silico*. This study is significant in observing the changes in viral load and clinical symptoms for the COVID-19 patients. It opens a new dimension to look towards Ayurveda as one of the important options to cure COVID patients.

Conclusion

In this study, NF2 was seen to provide a complete recovery from most of the clinical features of COVID-19 faster, when compared to the control. A high rate of conversion of RT-PCR from positive to negative was seen in 5 days in NF2 arm. Significant improvements were seen in the clinical symptoms of sputum formation, sore throat, headache, joint pains, fatigue, runny nose, loss of smell and loss of taste, after 5 days and 10 days of treatment with NF2 and standard of care treatment, in comparison to placebo with standard treatment. NF2 can be a part of cost effective integrated treatment therapy for managing NF2.

Declarations

Data Availability: The individual patient level data can be accessed at the following link https://docs.google.com/spreadsheets/d/1keaMxG6JblvyGV1n7EMbK8Yo_WaJbAiPeDj_KTHvpiQ/edit#gid=0

Ethics approval and informed consent:

The trial was conducted at Sri Sri College of Ayurvedic Science & Research Hospital, Sri Sri University, Cuttack, Odisha. The study was approved by the Institutional Ethics Committee, Sri Sri University (IEC Number-SSCASRH/IEC/001/21) and registered with CTRI No. CTRI/2021/08/036025.

Data availability:

The data that support the findings of this study is available from the corresponding author upon reasonable request.

Funding

No funding was received.

Conflict of interest

The test resources were provided by Sri Sri Tattva, /Sriveda Sattva Pvt Ltd, India. Dr Ravi Reddy is the chief scientific officer of Sriveda Sattva Pvt. Ltd., In addition Dr. Hari Venkatesh is the Research and Development head at Sriveda Sattva Pvt. Ltd. Besides providing the Intervention materials, Sriveda Sattva Pvt Ltd. was not involved in any aspect of this study. All the other authors have no conflicts of interest to declare.

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Supplementary Table

Supplementary Table 1: Assessment of Specific Clinical Features of COVID-19 Patients

ILLNESS		SEVERITY	GRADE
Fever		A febrile	0
		Mild fever (98.6E-100E)	1
		Moderate fever (100E- 103E)	2
		Severe (>103E)	3
Cough	Dry	Absent	0
		Mild dry cough only at morning and evening time	1
		Dry cough at any time	2
		Unable to sleep due to severe dry cough at night	3
	Sputum	Absent	0
		Thin and scanty	1
		Expectoration of thick sputum during coughing	2
		Expectoration of thick & yellow sputum	3
	Haemopt ysis	Absent	0
		Mild (<30ml)	1
		Moderate(30 -100ml)	2
		Severe(>100ml)	3
Sore throat		Absent	0
		Complaints of sore throat only on asking	1
		Complaints of sore throat on his /her own	2
		Change of voice associated with throat pain	3
Runny nose		Absent	0
		Sometimes watery secretion from nose	1
		Most of the times watery secretion from nose	2
		Always watery secretion from nose, and patient feels discomfort	3

Shortness of breath	Absent	0
	Present in resting condition	1
	Present after little work	2
	Present after moderate to heavy work	3
Headache	No Headache	0
	Occasional headache	1
	Can be tolerated without medication	2
	Uncontrolled headache	3
Fatigue	Patient can do his /her normal work	0
	Patient is able to do routine work with weakness	1
	Patient is able to do routine interfere the physical working	2
	Patient cannot do his normal work	3
Loss of smell (Anosmia)	Absent (Normal Smell)	0
	Mild Hyposmia	1
	Moderate Hyposmia	2
	Anosmia	3
Loss of Taste (Ageusia)	Normal Taste	0
	Mild Ageusia	1
	Moderate Ageusia	2
	Ageusia	3
Joint Pain	No pain in walking, sitting, standing and slipping)	0
	Pain in going up and down stair	1
	Pain in sitting and standing	2
	Pain in walking, sitting, standing and slipping)	3

Figures

Figure 1

CONSORT FLOW DIAGRAM