

The Effectiveness of Integrative Treatment Interventions on Covid-19 Patients:

A Single Group Pretest Posttest Clinical Trial.

Interagative Treatment of COVID-19: A single group clinical trial

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Abstract

World Health Organization (WHO) declared COVID-19 as pandemic on 11th March, 2020 and has affected every sphere of the life matrix from micro to macro levels. Individuals have suffered anxiety, depression and fear of death while countries undergone disruption and brutal economic recessions, it is still a global primary concern as dilemma of unavailability of cure both in conventional as well as unconventional medicines, however, relevant literature suggested prophetic, complementary, alternative and integrative medicine as speedy possible means to find a cure. Based on similar literature the aim of this study was to evaluate clinical effectiveness of integrative treatment intervention for COVID-19 patients.

The study design was a Single Group, Pretest-Posttest clinical trial, using purposive sampling of 34 (25 men and 9 women) COVID-19 infected patients, aged between 18 to 80 years, and enrolled over 4 months. The intervention treatment administered herbal compound drugs

twice a day and natural supplements to enhance immunity, with follow-up for a maximum of 13 days. The measured outcome was change in symptoms before and after intervention.

Paired Sample t-Test was applied and there was significant difference (.000*) between means of pre and post intervention outcomes. The integrative treatment was found to be effective and the success rate was 100 %, recovery period ranged from 3 days to maximum of 13 days.

The study suggests that a comprehensive integrative treatment plan, based on combination of various organic herbs and appropriate nutrition supplementary diet contributes in benefitting in effectively treatment of corona infection. Further, conduct RCTs and conduct Phase-2 trials to ascertain generalization, reliability and validity across larger population using larger sample size, diverse ethnicity, across geographical location. Subsequent studies can also probe to answer novel questions as to why and how the medicine affects SARS-CoV2 (COVID-19) at cellular and molecular level.

Keywords:

Prophetic (PBUH) Medicine (Al-libb Al-Nabawi), PAK-20, Oniater, Datseed, Integrative Medicine, SARS-CoV-2, Corona Virus, COVID-19, Dietary therapy.

1. INTRODUCTION

The speedy widespread of untreatable COVID-19, is still a global primary concern, that has effected almost every sphere of life. (Modi et al., 2020) Countries around the world have suffered extensive disruption, millions have been infected and also economies have undergone brutal recessions. The declared pandemic outbreak was initially identified as a cluster of pneumonia cases, of unknown etiology, in Wuhan, Hubei Province, China. (Liu et al., 2020) The outbreak has not only affected various dimensions and levels of life matrix, yet also induce a broad range of psychological contagion such as; fear, anxiety and depression on massive scale. (Liu et al., 2020).

As per the global data reported on 22nd June, 2020, the total cases reported worldwide were 9,072,657; in Turkey 187,685, in China 83,396, in India 426,910, in Pakistan 181,088 and in Iran 207, 525.

Presently there are two major fields contributing towards healthcare i.e., conventional and the unconventional medicines. Unconventional medicine is centuries old and has a wide range of variants, such as; Alternative Medicine (AM), Complementary Medicine (CM), Complementary and Alternative Medicine (CAM), Integrated Medicine or Integrative Medicine (IM), Holistic Medicine (HM), Traditional Chinese Medicine (TCM), Traditional & Complementary Medicine (T&CM), Traditional and Complementary and Integrative Medicine (TCI), Homeopathy, Ayur-

veda, Diet Therapy and Prophetic (PBUH) Medicine (Al-libb Al-Nabawi)/Islamic Medicine/ Traditional Arabic and Islamic Medicine (TAIM). (Al-Jauziyah, 1999; Babar, Syed, Naing, & Hamzah, 2012; Chopra & Doiphode, 2002; Pormann & Savage-Smith, 2007) On the contrary, conventional medicine is newly born (19th century) but took a lead in the 20th century when discovery of antibiotics claimed eradication of many diseases.

Since the outbreak of COVID-19 till present, the dilemma of unavailability of an approved effective treatment still exists, both in conventional as well as unconventional medicines. The success claims made so far have been scientifically objected and have not been approved by the world's renowned official scientific medical health regulatory organizations. (Panyod, Ho, & Sheen, 2020) Conclusively, the efforts to find a cure are still ongoing.

In few partial success claims made by TCM studies in China; (Chen et al., 2020) In 2019; a study used TCM named Shufeng Jiedu Capsule (SFJDC) on four COVID-19 patients and three gained significant improvement. (Wang, Chen, Lu, Chen, & Zhang, 2020) Similarly, a case study conducted in Wuhan, used SHL (Shuang-Huang-Lian; a three herbs TCM) on corona infected patients, resolved majority of symptoms on the 6th day. Further, two repeated 2019-nCoV test results showed negative. (Zandifar et al., 2020) Another similar study conducted in 2019, in Chinese used TCM; Yin Qiao San and Sangju Yin. Yin Qiao San, was given to relieve high fever and Sangju Yin was given to cure severe cough, clear lung heat and expel phlegm in order to achieve normal lung's function. ⁽¹¹⁾In several other alike studies, scientists researched to observe TCM medicines response to anti-SARS-CoV activity, and claimed

partial success yet were objected on scientific research criteria. (Cragg & Newman, 2013; Yang, Islam, Wang, Li, & Chen, 2020).

Similarly, several Randomized Controlled Trials (RCTs) were conducted by conventional medicine; however results categorized the allopathic/ pharmacologic medicines/ therapies as ineffective, for treating COVID-19 patients. (López-Alcalde, Yan, Witt, & Barth) Additionally, few recent clinical studies showed several treatments associated adverse effects as well. (Elhusseiny, Abd-Elshahed Abd-Elhay, & Kamel, 2020) Conclusively, in the existing literature, COVID-19 officially is still considered as incurable, and emphasis is being laid on conducting more clinical researches. (López-Alcalde et al.).

On the contrary, in the existing literature there exists substantial knowledge on efficacy of herbal, botanical and unconventional medicines, in numerous health dimensions. Substantially, the world's renowned scientific medical health regulatory organizations as well, do not reject evidence based viable effectiveness of herbal medicine and dietary therapies. Supplementary, recognition of their antimicrobial, antiviral and immunity enhancement effects as well. (Hasan & Mohieldein, 2016) Several studies suggested vitamins "C" and vitamin "D" of having potential to reduce the risk of corona infections. (Basiri, 2020; Parvin, Islam, Urmy, & Ahmed, 2020) However, no study suggests a single herb / extract / bioactive herbal compound as cure. Nevertheless, numerous authors are of the opinion that herbal compounds along with fitting nutrition management can be an effective and rapid approach towards COVID-19 infection treatment.

Correspondingly, Nigerian natural herbal remedies also suggest effective treatment of CO-

VID-19 infection by using botanical detoxifiers, immune boosters, natural antioxidants, plant haematinics and spices. (I. T. Gbadamosi, 2020). The valuably regarded botanicals/ detoxifiers are; Neem (*Azadirachta Indica*) and Turmeric (*Curcuma Domestica*). (I. T. Gbadamosi, 2020). Herbal immune boosters are; Guava (*Psidium Guajava*) leaf, Mango (*Mangifera Indica*) stem bark and leaf, Lemon grass leaf (*Cymbopogon Citratus*), Ginger (*Zingiber Officinale*) rhizome, Garlic (*Allium Sativum*) bulb and Cinnamon (*Cinnamomum Zeylanicum*). (I. T. Gbadamosi, 2020).

Likewise, several spices are also rich in antioxidants, antimicrobials and have anti-cancerous properties. It has been reported that a use of small amount of ginger (*Zingiber officinale*) daily for minimum of 11 days can reduce muscle pain, inflammation and aids digestion as well. (I. Gbadamosi, Moody, & Yekini, 2012).

Various herbs have also been scientifically researched and suggested for multiple clinical benefits e:g black Pepper (*Piper Nigrum*) is recommended effective in treating asthma, chronic indigestion, colon toxins, obesity, sinus, congestion, fever, intermittent fever, cold extremities, colic, gastric ailments and diarrhea. (Ghori & Ahmad, 2009) Also Fresh ginger dose restrain human respiratory syncytial virus -induced plaque formation. (San Chang, Wang, Yeh, Shieh, & Chiang, 2013) Similarly, clove is good expectorant as well as anti-viral agent that promotes the discharge of mucous and secretion in the respiratory passage. (Milind & Deepa, 2011) Equally, Cinnamon bark has been established effective against all the investigated pathogens. Clove oil in liquid medium present best inhibition against methicillin-resistant *Staphylococcus aur-*

eus (MRSA). (Ács, Bencsik, Böszörményi, Kocsis, & Horváth, 2016) In like manner, Fennel seeds (*Foeniculum Vulgare*) stimulate ciliary motility of the respiratory tract, and found effective in treating bronchial and bronco-pulmonary afflictions. Species such as clove, cinnamon, rosemary, paprika, nutmeg, ginger, garlic, mustard have antioxidant activities. They also have capability to detoxify the liver, act as anti-inflammatory and infectious protector agent. (Widowati, 2015) In Similar manner Jaivritri (*Myristica Fragrans*) extracts are effective for respiratory conditions such as cough, asthma, and dyspnea. (Rathi, Rajput, Gokarn, & Mehakarkar).

Another very effective natural organic medicinal field; the Prophetic (PBUH) Medicine, also known as TAIM is compilation of advices of Holy Prophet Muhammad (PBUH), on usage of natural resources / herbs for cures and remedies of various sickness, diet, hygiene & mental health. TAIM is the least expensive and most effective way of treating various physical and mental diseases/ disorders. It has been a great inheritance of Muslims for centuries, however, is gradually fading away due to lack of interest, research and believing it to be outdated in comparison to conventional medicine. (AlRawi et al., 2017).

COVID-19 though still remains incurable, yet researchers still endeavor to find a cure within the frameworks relevant to their respective fields. On the contrary it has been collaborative scientific trial studies integrating CAM and CM is another option. (Organization, 2019) This approach of integrative medicine is gaining rapid popularity with a perceived potential of being one of the effective methods to address treatment of COVID-19. Few evidences from clinical practice have demonstrated that integrating Western and traditional Chinese medicine played an important

role for China's successful battle against COVID-19. (Ni et al., 2020) Likewise, Brazil's national policy for unified health system, has also added integrative and complementary practices that includes; homeopathy, TCM, T&CM, acupuncture, medicinal plants and herbal medicines, anthroposophy medicine and social thermalism. (Organization, 2019) Forgoing in view, there is an equally essential need for a viable integrative treatment model that could lead to an effective COVID-19 treatment.

2. MATERIALS AND METHOD

2.1. Foundation Framework of Study

Integrative health care (IHC) is relatively a newer innovative approach towards health care delivery and is gaining increased center of attention. Several integrated health care models have been suggested along with derived approaches, across a broad range of frameworks and settings. However unanimously accepted definitions and conceptual model/ approach for COVID-19 treatment is still awaited. The design of this study is anchored to the IHC Model (Fig. 1).



Fig-1. KRIC's COVID-19 IHC Model Constructs Model (Source: courtesy of KRIC, 2020).

This suggested by KRIC as foundation along with derived COVID-19 Integrative Treatment Constructs Model (Fig. 2), KRIC Integrative Treatment Approach Model (Fig. 3) and treatment plan/ protocol (Fig. 4), to test the effectiveness of integrative treatment interventions on Covid-19 Patients in a clinical trial.

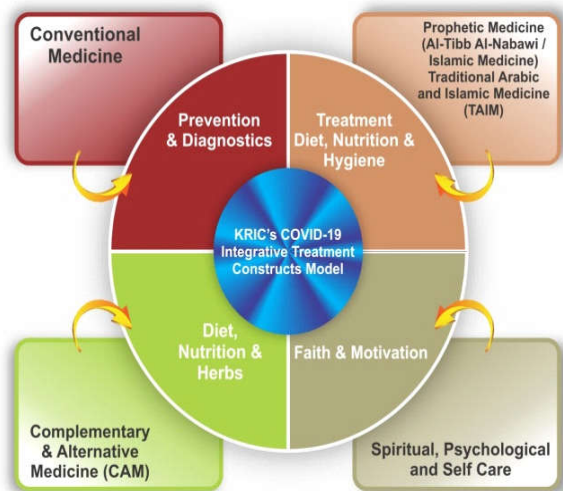


Fig-2 KRIC's COVID-19 Integrative Treatment Constructs Model.

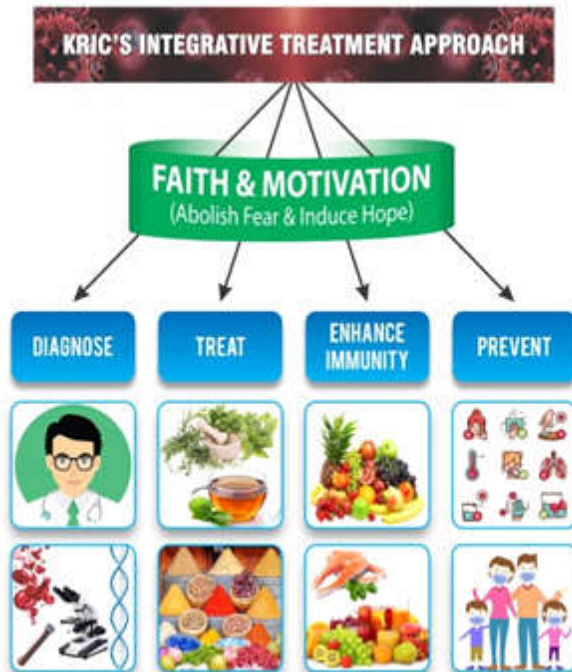


Fig-3 KRIC Integrative Treatment Approach Model

2.1.1. KRIC's Integrative Health Care Model

KRIC's IHC Model developed is based on four dimensions; CM, CAM, TAIM and SPSC (Spiritual, Psychological and Self Care) as reflected in Fig-1.

2.1.2. KRIC's COVID-19 Integrative Treatment Constructs Model

KRIC's COVID-19 Integrative Treatment Constructs Model (Fig.2) derived from KRIC's IHC Model (Fig.1). The required constructs from respective fields are selected.

2.1.3. KRIC's Integrative Treatment Approach Model

KRIC's COVID-19 Integrative Treatment Approach Model is represented in Fig.3. KRIC's Integrative Treatment Approach Model (Fig. 3), simultaneously addresses five facets. First; **“Faith & Motivation”**, which informally counsels the patient to relieve fear and invoke hope for cure. Second; **“Diagnose”** formulates diagnostic protocols in-line with conventional medical healthcare. Third; **“Treat”** furnishes treatment protocols using TAIMS/ herbal medicines. Fourth; **“Enhance Immunity”** uses appropriate diet management and natural supplements with essential nutrition form TAIMS and nutrition sciences. Fifth; **“Prevention”** educates the patient, attendant and others to take necessary preventive measures for own as well as other's safety as per guidelines of Center of Disease Control.

2.2. Inclusion and Exclusion Criteria

The experiment was conducted on ptest and posttest, the duration of the study was 4 months in which 34 COVID-19 infected patients were participated. Following were the inclusion

and exclusion criteria of the study.

2.2.1. Inclusion Criteria

Both Genders, Aged between 18-80 years, Active symptomatic and diagnosed patients, Mild, Moderate or severe infection, COVID-19 positive on the basis of symptoms, physical tests and lab tests.

2.2.2. Exclusion Criteria

Any tumor or malignancy, recent surgery, a. Patient on invasive / non-invasive ventilator (critical), Use of any other medicine parallel interventional medicines (PAK-20, Oniater and Hing) for treatment of COVID-19, Taking any immunosuppressant.

For:	Two-sided confidence level(1-alpha)	95		
	Power(% chance of detecting)	80		
	Ratio of Controls to Cases	1		
	Hypothetical proportion of controls with exposure	40		
	Hypothetical proportion of cases with exposure:	0.27		
	Least extreme Odds Ratio to be detected:	0.00		
	Kelsey	Fleiss	Fleiss with CC	
Sample Size - Cases	16	15	20	
Sample Size - Controls	16	15	20	
Total sample size:	32	30	40	
References				
Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15				
Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 & 3.19				
CC = continuity correction				
Results are rounded up to the nearest integer.				

Fig- 4 Sample Size (Kelsay)

2.2.3. Trial Registration

This trial is registered with IRCT (Iranian Registry of Clinical Trials), a Primary Registry in the WHO Registry Network.

IRCT registration number:

IRCT20200823048495N1

2.2.4. World Health Organization Unique Identifier for Clinical Trials

a. Displayed on the WHO International Clinical Trials Registry Platform’s (ICTRP) Search Portal(*Universal Trial Number/ UTN*):

b. WHO Universal Trial Number:

UTN U1111-1262-7419

2.2.5. Sampling Technique and Size

Sampling Technique is Purposive Sampling and size is N=34 (Kelsay) after adding 10% drop out.

2.2.6. Data Collection

Data of patients were collected on self-administered questionnaires which were completed in the beginning and at each alternate day till 14 days. This information was kept in

patients' data files.

2.2.7. Data Treatment

Out of 39 patients, 5 were excluded for falling into exclusion criteria due to non-adherence to the treatment plan. N=34 patient's information was added into the data file that was available for the analysis.

2.2.8. Ethical Considerations

Patients were fully informed about the aims and procedures of the study, and informed consent¹ was obtained. The study protocols were reviewed and approved by the Ethical Committee at KRIC.

2.2.9. Treatment Protocols

KRIC's Integrative Treatment Plan/ Protocols were used (described in Fig. 5) which elaborates the complete trial intervention segments. Experimental group was given baseline treatment; 1g of PAK-20² (containing cloves, Black pepper, Cumin Seed, Cinnamon, Black cardamom, Mace Spice, Nutmeg, Star anise and Bay leaves) in 250ml of Combo-1² (soup/meat stock) twice a day for a maximum of 12 days. Oniater¹ (onion water) 50 ml, once a day was given for consecutive 3 days. Hing² (Asafoetida) tempering (ground spices briefly roasted in oil) added to any food dish was given to those patients who developed blood clotting, or coagulation.

Treatment was given in parallel to enhance immunity and address nutrition efficiency; 250ml of Combo-2 (herbal tea) containing cloves, black pepper, green cardamom, black cardamom, stick of cinnamon, ginger slice, fennel seeds and half lemon juice twice a day for a maximum of 12 days. Datseed containing date filled with black seed (kalonji) was given once a day for a maximum

of 12 days. Datseed containing date filled with black seeds (kalonji) was given once a day for a maximum of 12 days. Use of fruits; such as apples, mangoes, pure organic juices; like carrot juice, orange juice, apple juice, mango milk shake even beyond 12 days until strength was restored. Meat/ lentils use for intake of proteins till recovery. Use 70gm of Talbina, once per day that increases 94 kcal, served as high potency oral multivitamins, high fiber and energy diet. (Badrasawi, Shahar, Abd Manaf, & Haron, 2013).

To address co-morbidities; Ajwa dates seed powder (market available herbal compound) was given to specifically those patients who were already suffering from diabetes, cardiovascular disease or hyperlipidemia (Hasan & Mohieldin, 2016; Khalid et al.). Homemade organic vinegar (one tea spoon in a glass of lukewarm water) was given empty stomach to patients with renal dysfunction, liver inflammation or heart blood vessel blocked, once a day for a maximum of 30 days. Heartburn/peptic ulcer was neutralized with Combo-3 (a yogurt and water mixture-based drink) and was spontaneously addressed.

2.2.10. Pre-Treatment Instructions to the Patients

All patients were intrinsically motivated in an informal counseling to minimize fear and induce hope of recovery, followed by pre-treatment instructions specific to the trial.

- a. Patients as well as attendant were advised to follow physical isolation and safety measures.
- b. They were instructed for strict adherence to the treatment plan as directed by the consultant.
- c. They were also asked to refrain from using any other kind of treatment/ medicine during the course of the study.
- d. Patients were asked to report their experienced regarding change in symptoms follow-up every day.

e. Patients were asked to refrain from self over/under dosing of high heat potency diets/medicine.

2.2.11. COVID-19 Pre and Post Assessment Tool /Questionnaire

KRIC's COVID-19 Scale is a self-developed tool used for Pre and Post Treatment Assessment.

2.2.12. Outcome Assessment

2.2.12.1. Primary Outcomes

Measuring symptoms' intensity; Fever was measured on thermometer scale, the intensity of Cough was measured on Visual Analogue Scale (VAS), Shortness of Breath was observed on Borg dyspnea scale (Ries, 2005), Muscle Pain was measured on VAS Scale (Hawker, Mian, Kendzerska, & French, 2011) and Throat Soreness was measured on sore throat scale. (Schachtel, Fillingim, Thoden, Lane, & Baybutt, 1988).

2.2.12.2. Secondary Outcomes

Measuring Effectiveness of the treatment; significance of mean difference of symptoms' intensity, from day one till day of recovery to a maximum of 12 days was measured.

2.2.13. Statistical Analysis

The analysis was done using SPSS version 21. Cronbach's Alpha was used to measure the reliability of questionnaire. Paired sample t-test was done to evaluate the outcome on symptoms before and after treatment. p-value <0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1. Reliability of KRIC's COVID-19 Scale

The self-developed questionnaire's reliability was tested on Cronbach's Alpha (Table 1).

Table 1. Reliability of Questionnaire

Cronbach's Alpha	No. of Items
0.757	33

3.2 Description of Demographic Data

3.2.1 Age

Mean age was 40.91±14.046

3.2.2. Age Statistics

As shown in Table no. 2, range of age was minimum 21 years and maximum 70 years of age.

Table 2. Age Statistics

Mean	40.9118
Median	38.5000
Std. Deviation	14.04617
Minimum	21.00
Maximum	70.00

3.2.3 Gender

79.4% (27) were males and 20.6% (7) were females.

3.3 Co-morbidities

Results showed that 70.6% (24) had no additional disease, while 2.9% (1) were already suffering from either one or combination of hypertension, peptic ulcer, liver diseases, renal diseases and hyperlipidemia, 11.8% (4) had diabetes and 5.9% (2) had asthma (Table 3).

3.4 Frequency of Symptoms Reported by Patients

Summary of the frequency of patient's

symptoms are given below in pictorial form in Fig-5.

Table 3. Summary of Co-morbidities

	Frequency (f)	Percent (%)
None	24	70.6
Hypertension	1	2.9
Peptic Ulcers	1	2.9
Liver Diseases	1	2.9
Diabetes	4	11.8
Asthma	2	5.9
Hyperlipidemia	1	2.9
Total	34	100.0

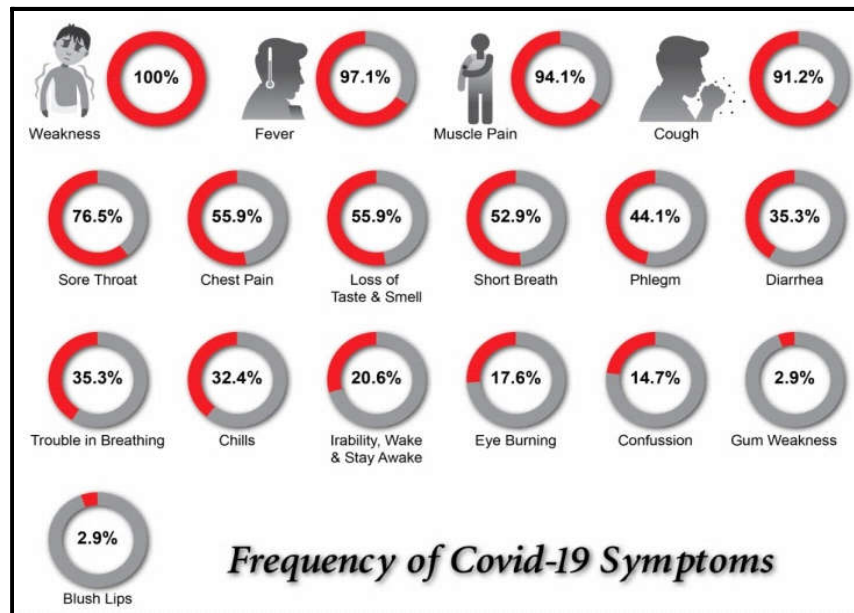


Fig-5 Summary of Frequency of Symptoms

3.5 Effectiveness of Integrative Treatment

Paired t-test was conducted to compare pre and post treatment effects at 95% of Confidence Interval (p-value < 0.05). The results

showed a significant difference between all Pairs (1,2,3,4,5 and 6) with p-value .000*. (Table 4). Paired t-test statistical analysis was applied

on all pairs which showed ; Pair 1 (cough before treatment vs cough after treatment) Mean was 4.8823 and SD=2.6142. Pair 2 (shortness of breath at rest before treatment vs shortness of breath at rest after treatment) Mean was 2.0882 and SD=2.0942. Pair 3 (shortness of breath during activity before treatment vs shortness of breath during activity after treatment) Mean was 2.1176 and SD=2.1986. Pair 4 (fever before treatment vs fever after treatment) Mean was 1.5588 and SD=0.5609. Pair 5 (muscle pain before treatment vs muscle pain after treatment) Mean was 4.7058 and SD=2.2767. Pair 6 (sore throat before treatment vs sore throat after treatment) Mean was 3.5882 and SD=2.8722.

Table 4. Summary of Paired t-TEST

		<i>Mean</i>	<i>SD</i>	<i>df</i>	<i>Sig.(2-tailed)</i>
Pair 1	Cough (Before-After Treatment)	4.8823	2.6142	33	.000*
Pair 2	Shortness of Breath at Rest (Before-After Treatment)	2.0882	2.0942	33	.000*
Pair 3	Shortness of Breath During Activity (Before-After Treatment)	2.1176	2.1986	33	.000*
Pair 4	Fever (Before-After Treatment)	1.5588	0.5609	33	.000*
Pair 5	Muscle Pain (Before-After Treatment)	4.7058	2.2767	33	.000*
Pair 6	Sore Throat (Before -After Treatment)	3.5882	2.8722	33	.000*

3.6 Principal Findings

The study showed successful results; the symptoms (cough, shortness of breath, fever, muscle pain and sore throat) resolved rapidly. The young adults and middle-aged patients 2.1176 recovered in 3-5 days, while old aged recovered in 7-9 days. Out of 34 patients 10 patients conducted post treatment confirmatory RT-PCR test and all 10 showed negative. Whereas the 10

patients conducted, post-treatment chest X-ray confirmatory test, which showed clear lungs. On the whole all 34 patients recovered on the basis of symptomatic relief.

PAK-20 and Oniater as an antiviral, antibiotic and anti-microbial drugs, showed quick effects. The given intervention of PAK-20 immensely relieved the patient from cough, phlegm and shortness of breath, by 3rd/4th day. Oniater (25ml) daily dose reduced the temperature from 102! (38.8 °C) to 99! (37.2 °C), on the 1st/2nd day and also relieved nausea and diarrhea. Paired t-test compared difference of means of pre and post treatment effects on symptoms (at 95% of Confidence interval, p-value <0.05), showed significant difference (p-value .000*).

While addressing co-morbidities, Ajwa dates seed powder proved to be an effective supplementary treatment for hypertension, heart disease, diabetes and hyperlipidemia patients. Hing/ Heeng (Asafoetida) proved to be very effective for hyperlipidemia, hypertension and Blood Coagulation patients. Combo 3 was very effective in neutralizing heartburn caused due to peptic ulcer/ self-extension/ overdosing of PAK-20.

Dietary and nutritional organic supplements especially Talbina, was effective for reliving weakness and fatigue. After the treatment the patients were asked about their satisfaction to integrative treatment plan; 85.3% graded the treatment as more effective while 14.7% graded as mildly effective.

3.7. Comparison with Previous Studies

The study approach was unique, effective, safer as well as economical. Only herbs and natural organic products were used. The treatment effectiveness was 100%, contrary to other studies

showing ineffectiveness/ limited effect of numerous pharmacologic treatment therapies, while treating COVID-19 patients.

As till date no drugs, monoclonal antibodies or vaccines have been approved to treat COVID-19 infected patients. Therefore, it successfully addressed the gap of non-availability of an effective treatment for COVID-19 infection.

The study used outcome measures for clinical trial in contrast to several other studies being critiqued of being observational and descriptive. The mass patients' recovery time was rapid (3-5) days as compared to SHL (Traditional Chinese Medicine) study conducted in Wuhan, China which resolved symptoms on the 6th day. (Ni et al., 2020) The study is aligned to a TCM study conducted in 2019, which used Yin Qiao San for patients to relieve high fever while this study used Oniater, moreover, TCM study used Sangju Yin to cure severe cough, clearing lung heat, expel phlegm to attain normal functioning of patient's lungs whereas this study used PAK-20.

The study addressed major critique on most of the CAM studies being conducted of being; observational, descriptive, very small sample size (less than 5), vaguely described given medicine compounds and the treatment received, recommendations were mainly established on the experts' experience and without provision of any supportive data. (López-Alcalde et al.) On contrary this study conducted a clinical trial, used a considerable sample size, medicine compounds given and the treatment received were clearly described and recommendations were established on comprehensive data analysis.

The study had very few mild side effects which appeared in a small number of cases mainly due to patient's non-adherence to the treat-

tment plan and co-morbidity. Whereas other studies stated treatment associated adverse effects including; respiratory failure and blood biomarkers of organ impairment, including low albumin, low potassium, low count of red blood cells, low count of thrombocytes and elevated bilirubin (jaundice), gastrointestinal distress, elevated transaminase levels in the blood (liver enzymes), infusion site reactions, and electrocardiogram abnormalities. (Elhusseiny et al., 2020).

3.8. Strengths of the Study

The key strengths of the study were; showed expeditious results of successful cure, with very short recovery period and almost negligible side effects, a safer/ easy/ economical treatment, also successfully addressed co-morbidities. Few reported unexpected findings were; significant relief from chronic cough, phlegm and post nasal drop, congestion, improved respiratory tract function and curing blood clotting. Other benefits include relief from depression, insomnia and anxiety.

3.9. Significance of the Study

The significance of this study is simplicity and cost-effectiveness of the treatment which can rapidly relief the world of COVID-19 pandemic. It suggests a self-developed outcome measurement instrument for COVID-19 patients. The study serves as a sound foundation for further unconventional confirmatory studies as well as conventional medicine physiological studies. The foundational KRIC's integrative healthcare model and treatment approach can be used to formulate integrative treatments for other diseases as well by incorporating conventional as well as unconventional guidelines, medicines, techniques, equipment and procedures.

3.10. Future Studies

Future studies may focus on clinical trials using the same Integrative Treatment on diverse populations with different ethnicity, across different geographical locations, with larger sample size, in different RCTs along with systematic reviews, probe for differences in pathophysiology (including environmental or social factors contributing to disease) and ascertain generalization, reliability and validity. Future studies can also probe novel questions as to why and how the medicine affects SARS-CoV2 (COVID-19) at cellular and molecular levels and what additional clinical benefits can be achieved. Subsequent studies can also contribute by suggesting improvement to the integrative model/ treatment.

An international collaborated and coordinated effort against COVID-19 pandemic may include imparting essential training to the trial team, ensuring; the excellence of consultants' skills to diagnose, prescribe, monitor, address co-morbidities, readjust medicine dose, frequency and diet, imparting information to the patient(s) attendant(s), ensuring quality preparation of the medicine on large scale and treatment under a collaborative umbrella to attain optimum results.

4. CONCLUSION

This study as a whole was a success providing a foundational basis to an integrative treatment approach and proceed further to RCTs and Phase-2 trials. The results from this study contribute to the existing literature of addressing management of corona virus infections.

This led us to conclude that a precise diagnostic, comprehensive integrative treatment plan, combination of different natural herbs,

supplemented by suitable diet containing appropriate nutrition contributes in benefitting bio-chemical changes to effectively treat corona infection.

Advanced researches shall further probe interaction of the medicine with COVID-19 virus at cellular and molecular levels and the clinical benefits.

Ethics Approval

The study protocol was reviewed and approved by the Ethical Committee at KRIC.

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Conflicts of Interests

The authors declare that there are no conflicts of interests.

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