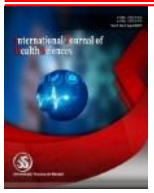

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Exploring Novel Risk Factors for Progression of Acute COVID-19 and Their Management Based on Ayurvedic Principles, with Emphasis on Diet-Lessons for Future Pandemics: A Retrospective Comparative Study

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Abstract

BACKGROUND: The COVID-19 pandemic hurled a huge avalanche of questions towards humanity and medical science, in terms of its understanding of new or emergent infections, the mechanisms for progression, and the spectrum of severity and their management in the absence of a proven anti-microbial. These questions shall always remain relevant due to the constant threat of the next pandemic. OBJECTIVES: This study intends to look at the factors discussed by ayurveda, as causes of progression to severe Jawara /infection, viz. whether presence of G.I symptoms like anorexia(indicative of agni-mandya), alone, or in combination with a disproportionate diet, and anxiety with insomnia(ca use of aama), can cause severe disease in acute covid-19 infected patients; and whether the modification of the diet as described in ayurvedic classics, alone, or in combination with medications, reduces its severity. METHODS: In this retrospective cohort study, 184 patients who attended the OP clinic at S.I.V.A.S, Hyderabad, across both waves of covid-19, were divided into two cohorts based on the A) presence of G.I symptoms like anorexia, nausea etc. and B) absence of GI symptoms and were studied in terms of the primary objective of, the impact of G.I symptoms alone or in combination with a diet disproportionate to one's appetite and anxiety with insomnia-on clinical and laboratory markers of severity of the disease. The impact of correction of the diet, alone or with ayurvedic medications, on mortality, clinical outcomes, and laboratory parameters was studied as the secondary objective. Multivariate Logistic regression analysis with R-studio was used to eliminate the impact of various confounding factors and odds ratios arrived at, with 95% C.I and a p-value of significance of <0.05 was used. RESULTS: The presence of GI symptoms (anorexia in particular) alone and more significantly in combination with the consumption of a disproportionate diet was associated with the incidence of a more severe/critical disease both clinically and by laboratory parameters. The correction of diet based on principles of jwara alone and in combination with ayurvedic medications resulted in significant reduction of morbidity, ZERO MORTALITY, and significant improvement of laboratory parameters. CONCLUSION: A 'heavy' diet consumed during the acute phase of COVID-19, when associated with anorexia, seems to play a significant role both in the pathogenesis of more severe/critical forms of the disease, and its removal and optimization of diet to one's appetite, alone or in combination with ayurvedic medications, seems to confer significant reduction in mortality and morbidity.

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1 Introduction

Background

COVID-19 has posed the largest challenge as of yet to the scientific community. As of March 2025, 778 million people across 232 countries were infected, with more than 7 million deaths being reported (https://data.who.int/dashboards/covid19/cases?n=o.last) apart from tremendous economic and ecological impact, with tons of medical waste-related microplastics generated (Talukdar et al., 2024). Although vaccination has brought down the disease incidence and severity, the emergence of new strains and possibly new viruses remains a dangling sword. Practically, it actually highlighted the challenge of new and emerging infections or future pandemics, with no known anti-microbials.

Understanding causative factors in disease pathogenesis and progression was a key challenge. A few risk factors are known, but although exhaustive, they do not explain disease progression in a large segment of patients with no known comorbidities, as was witnessed in a large number of young covid patients in the second wave.

The role of host factors, which are the most important determinants of progression, given the paradox of the same virus causing asymptomatic to critical illnesses, is yet to be understood fully. Ayurveda, with millennia of history and exposure to pandemics, approaches a host response-centric approach towards infections rather than a germ-centered approach and gives some of the best hypotheses for understanding and modulating host response (Adluri & Tripathi, 2022). With specific reference to COVID-19, the authors have maintained that COVID falls under the category of Saama Vaata jwara (Adluri & Tripathi, 2022) in the initial stages, and hence Aama plays the central role in its pathogenesis of inflammation and hypercoagulation, while vata causes the lung fibrosis, etc.

Agnimandya, or sluggishness of metabolism indicated by clinical symptoms of anorexia, dyspepsia, or, in severe cases, by nausea, vomiting, or loose motions, is explained as central to the manifestation of many diseases, including infections. This is posited to be due to the production of partially metabolized intermediates called AAMA (unripe) [ref. Madhav Nidan] from the food consumed, which could play a role either in encouraging the growth of microbes by playing a nutritive role for them, or inducing host inflammation, or both. Consumption of foods deemed as 'Guru' or 'Ati snigdha' like foods rich in fats, insoluble fiber, or mucilaginous content, or even simpler foods or liquids, in relatively large amounts, is described to increase this process [ref.10, chi. 3/138-chakrapani commentary,195]. A mind overwhelmed with emotions like fear, anxiety, etc., or insomnia is said to have a compounding effect on this process by worsening the agni [brain – gut axis] and thus increasing the progression of infections (Murthy KRS, 2000). Ama is thus deemed as one of

the chief causes of inflammation in infections in the short run and autoimmunity in the long run (Adluri & Bhattacharya, 2022).

Hence, huge importance is attached to the nutritional management of infections as well as autoimmunity in Ayurveda. Reducing the load of the ama precursor by judicious fasting or balancing the diet, so that it is proportionate to the person's appetite [langhana or apatarpana] in the initial management of fevers (nava jwara) is given paramount importance (Murthy KRS, 2000; Sharma, 2011). This process is supported by the addition of water boiled with herbs, stimulating digestive fire or agni, and later by medicated soft and light diet [yavagu], and much later by medications which stimulate the metabolism or agni [deepana] and digest the ama [pachana] so as to facilitate its elimination. [shodhana].

In fact, the use of medications was considered secondary, while nutritional management was considered primary, as 'Nidana parivarjana' or removal of the cause is said to be the main course of action in all diseases (Sharma, 2005). But this all-important aspect has not been adequately evaluated either by the modern medical or ayurvedic community of researchers, in their pursuit of a 'magical pill' which still remains elusive.

This study aims to fill this very important void by attempting to evaluate new risk factors for progression of disease in the light of ayurvedic principles like presence of gastro-intest inal symptoms viz. anorexia, nausea, vomitings and loose motions, and signs like coated tongue etc., (all of which indicate Agnimandya and amaavastha) in addition to consumption of guru ahara, and presence of insomnia and anxiety as described(both of which were commonly seen during the pandemic) above. The impact of correcting the diet, including fluids based on the principles of jwara management and the use of certain medications, on the various biochemical and clinical outcomes is intended to be looked at.

2 Materials and Methods

Study design

The present study is an open labeled retrospective cohort study with two limbs/objectives from among the out-patient records of subjects treated at the Centre for fever and respiratory symptoms, between June 2020 and 2021 October, 351 consecutive patients with proper documentation were selected and their records were screened for inclusion criterion.184 patients met the criterion (91 in first wave and 93 in second wave) and were included in the study, rest were excluded (167). These patients were divided into 2 cohorts/sub-groups with and without exposure to the suspected

causative factor. For the primary objective, thus separate pairs of cohorts/sub-groups were drawn for the presence/absence of GI symptoms in general and Anorexia in particular, for consumption of a diet disproportionate to appetite, the presence of anxiety enough to cause disturbance of sleep or insomnia, and the combination of all three. For the secondary objectives, separate pairs of cohorts/sub-groups were created for patients who showed good compliance to the prescribed ayurvedic diet, who took ayurvedic medications for 5 or more days, patients who followed both the ayurvedic diet and medications, and their opposites.

Potential confounding factors for both objectives were identified and their effect neutralized by multivariate regression analysis. The effect of exposure to these suspected causative factors was evaluated by measurement of various end points for both primary and secondary objectives. The relative risks/odds ratios were calculated along with confidence intervals and P values, and conclusions drawn.

Setting and duration

The data were collected retrospectively from the records of the patients who consulted SIVAS Health and Research Centre at Hyderabad, physically or online, between June 2020 and October 2021.

Inclusion criterion

All consecutive patients presenting with fever and respiratory symptoms during June 2020 to October 2021, who met the following criteria, were included.

1) Above the age of 16 yrs
2) Actively symptomatic with fever and or respiratory symptoms
3) Proven covid positive through RT-PCR, rapid antigen, or High-resolution CT- Chest.

4) Who had undergone laboratory or biochemical evaluation initially and at least at one follow-up.
5) Who had at least 1 or more follow -ups.
6) Who had a detailed dietary and other history recorded?

Exclusion criterion:
The following patients were excluded from the study
1) Children under age of 16
2) Patients with asymptomatic infection or presenting 3 weeks after the last active infective symptom or post covid symptoms
3) No laboratory confirmation of covid
4) No biochemical evaluation initially and at least on one follow up
5) lost or inadequate follow ups
6) Insufficiently documented history

Definitions of cohort sub- groups
For primary objectives
a) *GI group:* patients with proven COVID, who had gastrointestinal symptoms of anorexia, nausea, vomiting, or loose motions at the time of initial presentation or at follow-up, were designated as the GI group.
Non-GI group: patients with proven COVID, without any of the above Gastrointestinal symptoms, were designated as the non-GI group.
b) *Anorexia group:* patients who complained of a reduction of appetite at initial evaluation or follow-up were designated as the Anorexia group. They were further categorized into 3 groups based on patients' subjective assessment as mild, moderate, or severe. Severe anorexia was also defined by the presence of nausea and or vomiting.
Non-anorexia group: consisted of the group of patients who did not complain of loss of appetite initially or during the follow-up period.
c) *Disproportionate diet group:* the patients who had consumed a diet described in ayurvedic classics as 'guru and ati-snigdha' translated as consisting of relatively high amounts of fats, chiefly saturated fats [milk, curd, egg yellow, non-vegetarian fats, coconut oil, cheese, butter, cooking oil, oil seeds, nuts etc.], insoluble fiber[millets, oats, jowar, ragi, brown rice, etc.], mucilagino us foods[banana, hibiscus sabdariffa leaves, taro or Colocasia esculenta root, avocado etc.], uncooked or raw foods, or any excessive fluid or food intake beyond one's thirst or hunger were defined as disproportionate diet group.
Proportionate diet group: patients who did not consume the items as stated earlier, and ate and drank proportionately to the dictates of their appetite and thirst were defined as the proportionate group.
d) *Anxiety group:* patients who complained of anxiety, which was severe enough to disturb their sleep or cause insomnia, were defined as the anxiety group.
Non-Anxiety group: Patients who did not complain of anxiety or had anxiety that was not severe enough to disturb their sleep were defined as the non-anxiety group.
e) *Combination group 1:* patients who had a combination of anorexia and disproportionate diet were called combination group 1
Non-combination group 1: All the patients who did not have the combination of anorexia and disproportionate diet were called non-combination group 1.
Combination group 2: patients who had a combination of GI symptoms, anorexia, disproportionate diet, and anxiety severe enough to cause insomnia were called combination group 2
Non-combination group 2: All the patients who did not have the combination of GI symptoms, anorexia, disproportionate diet, and anxiety with insomnia were called non-combination group 2.

For secondary objectives
a) *Good dietary compliance group:* the group of patients whose 24-hour dietary recall at follow-up showed that the patient followed the given dietary advice on all 3 meal times was included in this group.

Average –Poor dietary compliance group: those patients whose 24-hr. dietary recall at follow-up suggested that they followed the dietary advice on only 2 meal times (average) or 1 or none of the meal times (poor) were included in this group.

b) *Ayurvedic medicines group:* Patients who used the prescribed ayurvedic medicines continuously for at least 5 or more days were included in this group.
Non-Ayurvedic medicines group: patients who did not opt to use or did not use ayurvedic medications prescribed for at least 5 days or more were included in this group.

c) *Combination group:* patients who showed good compliance with the ayurvedic diet on follow-up and also used ayurvedic medications for at least 5 or more days were included in this group.
Non-combination group: patients who showed an average or poor compliance to diet advised at follow-up, and also did not opt to use, or used ayurvedic medicines for less than 5 days, were put in this group.

Other criterion

Risk factors for progression

The disease was identified as per CDC criterion [4] and was further subcategorized as follows

- Very mild- with no known risk factors
- Mild, with only 1 risk factor (excluding age more than 65)
- Moderate – with at least 2 risk factors
- Severe- with 3 or more risk factors.

Coating of tongue severity

The coating of tongue severity was based on a self-developed scale, as follows

- Grade-1 –tongue coated, but the normal pink color of the tongue is still visible through the coating
- Grade 2- tongue coated- normal color of the tongue(pink) not visible through the coating.
- Grade 3- coating of grade 2 but associated with a color change of the coating material to yellow, brown, or black.

Patterns of coating, like central, peripheral, or both, were also recorded.

Disease severity at presentation

The severity of COVID-19 was graded as per the NIH classification[12]

- ***Asymptomatic or presymptomatic infection****:* Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.
- *Mild illness:* Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- *Moderate illness:* Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO_2)≥94% on room air at sea level.
- *Severe illness:* Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.
- *Critical illness:* Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Interventions used

Ayurvedic diet (Adluri & Tripathi, 2022)

Patients were instructed to eat strictly according to appetite. i.e.- if nauseated or vomiting (severe anorexia)- fasting for 8 to 12 hours, if appetite very low but no nausea (moderate anorexia) -thin soups or ganji or rice soup, if appetite low (mild anorexia)- thin porridge made out of rice and green gram or wheat boiled with medicated water (yavagu), if appetite normal or no anorexia- soft rice with curries of fruiting vegetables(not roots), thin dal, rasam, non-spicy pickle or pulkas.

Ayurvedic water
Normal drinking water was boiled with a suitable herb like coriander seeds, dry ginger, trikatu, or shadanga paniya churna (10 to 15 gms for every 1 liter of water) till the water reduced to 750 ml. This was advised to be used for drinking and cooking.

Ayurvedic medicines (Adluri & Tripathi, 2022)
Ayurvedic medicines were prescribed based on the clinical features and generally included

1) Sudarshana kalpas (Ghana vati, tablets or churnam)–chandra prakash ayur sansthan, Gorakhpur, or Dabur,
2) Tribhuvana kirti ras-sree dhootpapeshwar ltd.,
3) Sanjeevani vati,- sree dhootpapeshwar ltd
4) Amrutarishtam-sandu,
5) Jayamangal ras- sree dhootpapeshwar ltd –only in high-risk group patients.

Severe cases with SOB received abhraka bhasma, suvarna bhasma, and shwasa kasa chintama ni-all of Sree Dhootpapeshwar Ltd.
Minor changes were made if warranted by the clinical situation to this regimen, and were documented. Dosages were based on the clinical condition, and duration was for at least 5 to 7 days, but was tailored to the clinical state of the patient.

Compliance with diet
Compliance with the diet was also recorded based on a self-developed scale as follows
Good- if the 24-hour dietary recall at follow-up showed that the patient followed the given dietary advice on all 3 meal times.
Average- if the patient followed the dietary advice at least 2 meal times.
Poor- if the patient followed the given dietary advice on only 1 or fewer than 1 occasion every day.

Days taken to functional recovery
Days taken to functional recovery were taken as the difference between the day of initiation of ayurvedic medicines and the day when the patient reported a subjective sensation of feeling better and returned to normal daily activities without any difficulty.

Objectives of the study –and end points

Primary objectives- the primary objective of the study was to test if there was any association/correlation between the presence of GI symptoms like anorexia, nausea, and vomiting, either alone
or in association with a disproportionate diet consumption and anxiety severe enough to cause insomnia, on the manifested severity of the disease.
Primary end points- the primary objective was sought to be established by the following endpoints.

1) Clinical severity of the disease was assessed as per the NIH criterion.
2) Severity of coated tongue.
3) CRP elevation.
4) D-Dimer elevation.
5) CT severity score, as per pan etal[13]. Each of the 5 lung lobes was visually scored from 0 to 5 as: 0, no involvement; 1, <5% involvement; 2, 25% involvement; 3, 26%-49% involveme nt; 4, 50%-75% involvement; 5, >75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement).

Secondary objectives – the secondary objective was to see if the diet was modified to suit the appetite of the patient as per the jwara principles described in Ayurveda, with or without concomitant Ayurvedic medications – it resulted in a better clinical outcome. (10, chikitsa.3/138-144)

Secondary end points – to verify the secondary objectives, the following end points were used

1) Mortality
2) Reduction of CRP after treatment
3) Reduction of D-Dimer after treatment
4) Total steroid requirement
5) Need for oxygen
6) Days taken for functional recovery
7) Hospitalization
8) Post covid sequelae

The following were also observed but not formally included: high flow oxygen, ventilator or ECM, or requirement RT-PCR status at 14 days after treatment remdesivir administration, Effect of Diet.

Statistical methods

Multivariate logistic regression analysis was done using R Studio to exclude the effect of various confounders on the measured outcome. The Odds ratio was calculated, 95% confidence interval (CI)was used, and a p-value less than 0.05 was deemed significant.

Confounding factors

For analysis of the primary objectives, the following were considered as potential confounding factors

1) Risk factors for the progression of disease or comorbidities
2) Vaccination (in 2nd wave)
3) Use of concomitant medications

While for the secondary objectives, the following confounders were considered in the analysis

4) Risk factors for progression of disease or comorbidities
5) Disease severity at presentation
6) Vaccination
7) Administration of remdesivir
8) Administration of steroids

The effect of these confounding factors was eliminated by multivariate regression analysis

3 Results and Discussions

3.1 Results

Participants

Three hundred and fifty-one (351) consecutive patients with proper documentation treated at SIVAS Health and Research Institute, Hyderabad, for fever and respiratory symptoms, between June 2020 and October 2021, were selected, and their records were screened for inclusion criteria. 184 patients met the criterion (91 in the first wave and 93 in the second wave) and were included in the study. The rest were excluded (167). 76patients of the 1st wave and 48 patients of 2 nd wave (total of 126) were excluded for insufficient data,27were excluded as they were late-post-COVID status without active infective symptoms,12 did not have laboratory-proven COVID, and 2 patients could not be identified for verification of data. Their latest health status was rechecked for any significant post-COVID complications through a telephonic call-up to October 2022 and recorded.

Baseline characteristics of patients

Table 1
Summary of Demographic and Baseline Characteristics of the Study

Parameter	Statistics	Overall
Gender	n	184
	Male	84 (45.65%)
	Female	89 (48.37%)
Age	n	184
	Mean ± Sd	51.25 ± 16.16
	Median	51.00
	Quantile	38.00;65.00
	Range	10.000 - 90.000
Height	n	184
	Mean ± Sd	1.65 ± 0.08
	Median	1.65
	Quantile	1.60;1.70
	Range	1.350 - 1.850
Weight	n	184
	Mean ± Sd	70.37 ± 12.41
	Median	70.00
	Quantile	62.75;78.00
	Range	42.000 - 110.000
BMI	n	184
	Mean ± Sd	25.65 ± 4.29
	Median	25.35
	Quantile	23.51;27.84
	Range	0.002 - 39.442

The mean age of patients across both the waves was 51.25(with a range of 16 to 90 yrs), with 51.6% (95) being males and 48.4 (89) females. The mean BMI of patients was 25.65 (± 4.29). Overall, in terms of comorbidities, there were 1(0.5%) very mild risk,97(52.7%) mild risk, 46(25%) moderate risk, and 40 (21.7%) high risk patients. The commonest comorbidities were elderly age (>65), hypertension, and diabetes. In terms of disease severity; 102 (55.4%) had mild disease,65(35.3%) had moderate ,11(5.98%) had severe disease and 6(3.3%) had critical disease. In terms of symptoms, there were 132 patients with GI symptoms (61 in 1st wave and 71 in 2nd wave) compared to 52 patients without GI symptoms (30 in 1st wave and 22 in the second wave). The frequency of the GI symptoms was as follows: anorexia-121(65.8%) patients (54- wave 1 and 67- wave 2), nausea-11(6%) patients (7- wave 1 and 4- wave 2), vomiting-21 (11.4%) (first wave -12, second wave-9), loose motions or altered stool frequency -47(25.5%) (22 -wave 1,25 in wave 2).

Distribution of potential confounding variables

For the measurement of primary objectives, the following were considered as potential confounding variables

1) Risk factors for progression of the disease or co-morbidities: very mild risk-1(0.5%), mild risk-97(52.7%), moderate risk-46(25%), high risk-40(21.7%)
2) Vaccination: Vaccinated -24 (13%), [covishield-12-single dose,5-double doses; covaxin-3-single dose,4-double doses], non-vaccinated-160 (87%)
3) The number of concomitant non-steroidal and non-antiviral co-medications received: No drugs-44 (23.9%), 1-3 drugs- 69(37.5%), 4-6 drugs - 49(26.6%), >6 drugs - 15(8.1%)

While for the secondary objectives, the following confounders were considered for analysis.

1) Risk factors for progression of disease or comorbidities
2) Vaccination
3) Disease severity at presentation: Mild- 102(55.4%), Moderate -65(35.3%), Severe-11(6%), Critical-6(3.7%)
4) Administration of remidesivir: Remedesivir-39(21.2%), No-Remedesivir-145(78.8%)
5) Administration of steroids: Steroids-63(34.2%), non-steroids-121(65.7%)

Outcomes for the primary objective

For the primary objective of potential risk factors that can affect severity, the following endpoints were measured:

1) Clinical severity of the disease assessed as per NIH criterion
2) Severity of coated tongue
3) CRP elevation
4) D-Dimer elevation
5) CT severity score, as per (Pan et al., 2020)

(GI group vs. non-GI group) The effect of GI symptoms on disease severity

GI symptoms were seen in 132 patients, while they were not seen in 52 patients. After adjustment for confounding variables, patients with GI symptoms had a much higher incidence of moderate disease, and almost exclusive incidence of severe and critical disease, with a very high odds ratio and also a significant p-value when compared to patients without GI symptoms. The CRP elevation had high odds, with a p value of 0.06, while D-dimer also showed higher odds for the GI group. HRCT showed a higher incidence, but it was not statistically significant, and the coating of the tongue did not show consistent results.

Table 2
GI group Vs. Non-GI group

Parameters		GI (132)	Non-GI (52)	Odds Ratio	95% CI	p-value
C-REACTIVE PROTEIN	CRP [0-6]	37 (28.03%)	22 (42.31%)	-	-	-
	CRP (>6,30]	51 (38.64%)	19 (36.54%)	1.68	(0.77,3.67)	0.19641
	CRP (30,60]	15 (11.36%)	4 (7.69%)	1.85	(0.51,6.65)	0.34607
	CRP (>60)	20 (15.15%)	2 (3.85%)	4.79	(0.93,24.64)	0.06084
D-DIMER	D-dimer [0-500]	65 (49.24%)	28 (53.85%)	-	-	-
	D-dimer (>500)	49 (37.12%)	13 (25.00%)	1.24	(0.55,2.82)	0.60313
DISEASE SEVERITY	Mild	60 (45.45%)	42 (80.77%)	-	-	-
	Moderate	55 (41.67%)	10 (19.23%)	3.19	(1.34,7.59)	0.00858
	Severe	11 (8.33%)	-	1.38×10^{12}	$(7.70 \times 10^{12}, 2.48 \times 10^{12})$	-
	Critical	6 (4.55%)	-	1.92×10^{08}	$(4.65 \times 10^{07}, 7.89 \times 10^{08})$	-
CT-SEVERITY SCORE	HRCT - 0	12 (9.09%)	2 (3.85%)	-	-	-
	HRCT - [1,8]	25 (18.94%)	11 (21.15%)	0.3	(0.05,1.72)	0.17721
	HRCT - [9,15]	15 (11.36%)	3 (5.77%)	0.55	(0.07,4.14)	0.55823
	HRCT - [16,25]	12 (9.09%)	1 (1.92%)	1.08	(0.08,15.27)	0.95213
COATING OF TONGUE - SEVERITY	Grade I (0.5 & 1)	60 (45.45%)	25 (48.08%)	-	-	-
	Grade II (1.5 & 2)	53 (40.15%)	17 (32.69%)	1.25	(0.58,2.71)	0.56987
	Grade III (2.5 & 3)	5 (3.79%)	1 (1.92%)	0.51	(0.04,6.37)	0.60353

Anorexia vs. non-anorexia group: effect of anorexia on disease severity

A total of 120 patients reported anorexia (mild- 61, moderate-47, severe-12) while 63 patients had no anorexia. Sub-group analysis was done for the different severities of anorexia. There was a higher incidence of moderate disease among all the subgroups of anorexia with a high odds ratio and a significant p. Also notable was the almost exclusive incidence of severe and critical disease

only in the anorexia group, with zero occurrence of severe and critical disease in the non-anorexia group. The CRP showed significant elevation in the anorexia group; d-dimer did not show a strong association. The HRCT showed an inconsistent association with anorexia, but there was a strong and statistically significant association between coated tongue and anorexia.

A subgroup analysis of the anorexia group into mild, moderate, and severe anorexia also showed a progressively increasing incidence of higher CRP, clinical severity of disease, higher radiological scores, and higher grade of coated tongue with increasing severity of anorexia.

Table 3
Anorexia & Non-Anorexia

			MILD ANOREXIA				MODERATE ANOREXIA				SEVERE ANOREXIA			
Parameters		**Non - Anorexia (63)**	**Anorexia - Mild (61)**	**Odds-mild**	**95% CI**	**p-value**	**Anorexia - Moderate (47)**	**Odds-moderate**	**95% CI**	**p-value**	**Anorexia - severr (12)**	**Odds-severe**	**95% CI**	**p-value**
CRP	1.C RP [0-6]	28 (44.44%)	17 (27.87%)	-	-	-	13 (27.66%)	-	-	-	1 (8.33%)	-	-	-
	2.C RP (>6,30]	23 (36.51%)	26 (42.62%)	1.95	(0.83, 4.58)	0.12374	17 (36.17%)	1.71	(0.65, 4.48)	0.27268	4 (33.33%)	6.22	(0.59, 65.16)	0.12704
	3.C RP (30,60]	5 (7.94%)	7 (11.48%)	2.16	(0.57, 8.22)	0.25743	6 (12.77%)	1.72	(0.4,7.5)	0.46862	1 (8.33%)	3.69	(0.17, 79.35)	0.40415
	4.C RP (>60)	2 (3.17%)	9 (14.75%)	6.51	(1.17, 36.31)	0.03251	5 (10.64%)	3.74	(0.59, 23.65)	0.16162	6 (50.00%)	39.53	(2.6,601.32)	0.00811
D-DIMER	D-dimer [0-500]	33 (52.38%)	36 (59.02%)	-	-	-	19 (40.43%)	-	-	-	-	-	-	-
	D-dimer	17 (26.	21 (34.43%)	0.91	(0.38, 2.16)	0.82838	18 (38.30%)	1.24	(0.48, 3.22)	0.65411	-	1.08	(0.24, 4.91)	0.91916

Parameters		Non-Anorexia (63)	MILD ANOREXIA				MODERATE ANOREXIA				SEVERE ANOREXIA			
			Anorexia - Mild (61)	Odds-mild	95% CI	p-value	Anorexia - Moderate (47)	Odds-moderate	95% CI	p-value	Anorexia - severe (12)	Odds-severe	95% CI	p-value
	(>500)	98%)												
DISEASE SEVERITY	Mild	51 (80.95%)	37 (60.66%)	-	-	-	13 (27.66%)	-	-	-	-	-	-	-
	Moderate	12 (19.05%)	21 (34.43%)	3.19	(1.34, 7.59)	0.00858	26 (55.32%)	0.89	(0.31, 2.54)	0.82518	-	4.26	(1.63, 11.16)	0.00314
	Severe	-	2 (3.28%)	1.38×10^{12}	$(7.7 \times 10^{11}, 2.48 \times 10^{12})$	-	5 (10.64%)	1.54×10^{9}	$(3.11 \times 10^{8}, 7.68 \times 10^{9})$	-	1 (8.33%)	1.14×10^{10}	$(3.67 \times 10^{9}, 3.57 \times 10^{10})$	-
DISEASE SEVERITY	Critical	-	1 (1.64%)	1.92×10^{8}	$(4.64 \times 10^{7}, 7.89 \times 10^{8})$	-	3 (6.38%)	0.14	(0.01, 1.92)	0.14106	-	0.46	(0.03,7)	0.57817
HRCT SEVERITY SCORE	HRCT - 0	2 (3.17%)	5 (8.20%)	-	-	-	5 (10.64%)	-	-	-	-	-	-	-
	HRCT - [1,8]	14 (22.22%)	13 (21.31%)	0.32	(0.05, 2.11)	0.23631	5 (10.64%)	0.12	(0.01, 0.96)	0.04615	-	0.13	(0.01, 1.76)	0.12544
	HRCT - [9,15]	3 (4.76%)	7 (11.48%)	0.61	(0.07, 5.56)	0.66354	7 (14.89%)	0.62	(0.06, 6.04)	0.67713	-	0.12	(0,3.14)	0.20067
	HRCT - [16, 25]	1 (1.59%)	1 (1.64%)	0.3	(0.01, 8.2)	0.47488	7 (14.89%)	1.78	(0.11, 29.43)	0.68824	-	1.15	(0.04, 31.23)	0.93439

COATED TONGUE	Grade I (0.5 & 1)	32 (50.79%)	28 (45.90%)	-	-	-	20 (42.55%)	-	-	-	1 (8.33%)	-	-	-
			MILD ANOREXIA				**MODERATE ANOREXIA**				**SEVERE ANOREXIA**			
Parameters		**Non-Anorexia (63)**	**Anorexia-Mild (61)**	**Odds-mild**	**95% CI**	**p-value**	**Anorexia-Moderate (47)**	**Odds-moderate**	**95% CI**	**p-value**	**Anorexia-severe (12)**	**Odds-severe**	**95% CI**	**p-value**
SEVERITY	Grade II (1.5 & 2)	18 (28.57%)	27 (44.26%)	1.64	(0.72, 3.74)	0.2402 7	20 (42.55%)	1.74	(0.7,4.34)	0.2329	-	1.81	(0.38, 8.69)	0.45611
	Grade III (2.5 & 3)	1 (1.59%)	-	-	-	-	3 (6.38%)	1.26	(0.09, 18.18)	0.86448	-	2.65	(0.09, 74.85)	0.56774

Effect of diet on disease severity (disproportionate diet vs. proportionate diet)

Overall, 146 people had a disproportionate diet, while 37 had a proportionate diet. Intake of Disproportionate diet showed the strongest correlation with all parameters of disease severity; with statistically significant incidence of moderate disease and exclusive incidence of severe and critical disease, when compared to subjects who had a diet proportionate to their appetite, after eliminating the effect of all potential confounders.it also showed statistically significant association with CRP elevation and again exclusive incidence of high HRCT severity score as well as severity of coated tongue, and a relatively small, higher incidence of raised D-dimer.

Table 4
Disproportionate diet Vs. Proportionate Diet

Parameters		**Disproportionate Diet (146)**	**Proportionate Diet (37)**	**Odds Ratio**	**95% CI**	**p-value**
CRP	CRP [0-6]	39 (26.71%)	20 (54.05%)	-	-	-
	CRP (>6,30]	59 (40.41%)	11 (29.73%)	2.81	(1.16,6.78)	0.02184
	CRP (30,60]	18 (12.33%)	1 (2.70%)	8.08	(0.97,67.56)	0.05381
	CRP (>60)	20 (13.70%)	2 (5.41%)	3.96	(0.75,20.88)	0.10482
D-DIMER	D-dimer [0-500]	74 (50.68%)	19 (51.35%)	-	-	-
	D-dimer (>500)	53 (36.30%)	9 (24.32%)	1.16	(0.45,2.98)	0.75719
Parameters		**Disproportionate Diet (146)**	**Proportionate Diet (37)**	**Odds Ratio**	**95% CI**	**p-value**
DISEASE SEVERITY	Mild	71 (48.63%)	31 (83.78%)	-	-	-
	Moderate	59 (40.41%)	6 (16.22%)	3.71	(1.3,10.57)	0.01404
	Severe	10 (6.85%)	-	1.92 x	(1.07 x 10^{12}, 3.45 x	-

				10^{12}	10^{12})	
	Critical	6 (4.11%)	-	5.62 x 10^{06}	(1.43 x 10^{06},2.20 x 10^{07})	-
CT SEVERITY	HRCT - 0	10 (6.85%)	4 (10.81%)	-	-	-
	HRCT - [1,8]	28 (19.18%)	8 (21.62%)	1.37	(0.3,6.17)	0.68088
	HRCT - [9,15]	18 (12.33%)	-	2.86 x 10^{07}	(1.34 x 10^{07},6.08 x 10^{07})	-
	HRCT - [16,25]	13 (8.90%)	-	1.87 x 10^{07}	(7.12 x 10^{06},4.91 x 10^{07})	-
COATED TONGUE SEVERITY	Grade I (0.5 & 1)	64 (43.84%)	20 (54.05%)	-	-	-
	Grade II (1.5 & 2)	66 (45.21%)	4 (10.81%)	5.07	(1.59,16.18)	0.00609
	Grade III (2.5 & 3)	6 (4.11%)	-	1.79 x 10^{21}	(2.76 x 10^{20} ,1.16 x 10^{22})	-

Presence of anxiety on disease severity

In all 41 patients reported anxiety, which was severe enough to disturb sleep during the infection, while 143 did not. Although anxiety showed some correlation with disease severity, CRP elevation, and severity of coated tongue, it was not consistent with D-dimer and HRCT scores.

Table 5
Anxiety enough to cause insomnia vs Non-Anxiety

Parameters		**Anxiety with insomnia (41)**	**Non-Anxiety with insomnia (143)**	**Odds Ratio**	**95% CI**	**p-value**
CRP	CRP [0-6]	13 (31.71%)	46 (32.17%)	-	-	-
	CRP (>6,30]	10 (24.39%)	60 (41.96%)	0.59	(0.23,1.56)	0.29092
	CRP (30,60]	5 (12.20%)	14 (9.79%)	1.52	(0.41,5.6)	0.53006
	CRP (>60)	7 (17.07%)	15 (10.49%)	1.81	(0.49,6.67)	0.37172
D-DIMER	D-dimer [0-500]	21 (51.22%)	72 (50.35%)	-	-	-
	D-dimer (>500)	12 (29.27%)	50 (34.97%)	0.68	(0.27,1.68)	0.40146
DISEASE SEVERITY	Mild	16 (39.02%)	86 (60.14%)	-	-	-
	Moderate	19 (46.34%)	46 (32.17%)	2.01	(0.82,4.93)	0.12709
	Severe	3 (7.32%)	8 (5.59%)	1.14	(0.17,7.81)	0.89622
	Critical	3 (7.32%)	3 (2.10%)	1.05	(0.1,11.02)	0.97007
CT-SEVERITY	HRCT - 0	4 (9.76%)	10 (6.99%)	-	-	-
	HRCT - [1,8]	13 (31.71%)	23 (16.08%)	0.98	(0.22,4.4)	0.97664
	HRCT - [9,15]	3 (7.32%)	15 (10.49%)	0.22	(0.03,1.45)	0.11491
Parameters		**Anxiety with insomnia (41)**	**Non-Anxiety with insomnia (143)**	**Odds Ratio**	**95% CI**	**p-value**
	HRCT - [16,25]	5 (12.20%)	8 (5.59%)	0.54	(0.08,3.48)	0.51621
COATED TONGUE SEVERITY	Grade I (0.5 & 1)	15 (36.59%)	70 (48.95%)	-	-	-
	Grade II (1.5 & 2)	20 (48.78%)	50 (34.97%)	2.09	(0.9,4.85)	0.08529
	Grade III (2.5 & 3)	4 (9.76%)	2 (1.40%)	5.58	(0.59,52.77)	0.13355

Combined presence of the above factors

The combination of Anorexia with a disproportionate diet was seen in 107 patients, with 77 showing a lack of this combination. This combination showed a very strong as well as a statistically significant correlation with disease severity, CRP elevation, HRCT score, coated tongue, and also showed a slightly higher incidence of raised D-dimers.

Table 6
Anorexia and disproportionate diet

Parameters		Anorexia+ Disproportionate Diet (107)	Non-anorexia + no Disproportionate Diet (77)	Odds Ratio	95% CI	p-value
C-REACTIVE PROTIEN	CRP [0-6]	25 (23.36%)	34 (44.16%)	-	-	-
	CRP (>6,30]	44 (41.12%)	26 (33.77%)	2.52	(1.18,5.35)	0.01644
	CRP (30,60]	13 (12.15%)	6 (7.79%)	2.43	(0.76,7.76)	0.1333
	CRP (>60)	18 (16.82%)	4 (5.19%)	4.47	(1.24,16.1)	0.02215
D-DIMER	D-dimer [0-500]	54 (50.47%)	39 (50.65%)	-	-	-
	D-dimer (>500)	40 (37.38%)	22 (28.57%)	0.92	(0.44,1.93)	0.83396
DISEASE SEVERITY	Mild	43 (40.19%)	59 (76.62%)	-	-	-
	Moderate	48 (44.86%)	17 (22.08%)	3.22	(1.5,6.9)	0.00263
	Severe	10 (9.35%)	-	3.75×10^{11}	(2.07×10^{11}, 6.76×10^{11})	-
	Critical	6 (5.61%)	-	6.11×10^{07}	(1.47×10^{07}, 2.54×10^{07})	-
CT-SEVERITY	HRCT - 0	10 (9.35%)	4 (5.19%)	-	-	-
	HRCT - [1,8]	18 (16.82%)	18 (23.38%)	0.36	(0.09,1.51)	0.1635
	HRCT - [9,15]	15 (14.02%)	3 (3.90%)	1.53	(0.26,9.1)	0.63863
	HRCT - [16,25]	12 (11.21%)	1 (1.30%)	3.19	(0.28,36.54)	0.35102
	Grade I (0.5 & 1)	42 (39.25%)	43 (55.84%)	-	-	-
Parameters		**Anorexia+ Disproportionate Diet (107)**	**Non-anorexia + no Disproportionate Diet (77)**	**Odds Ratio**	**95% CI**	**p-value**
COATED TONGUE SEVERITY	Grade II (1.5 & 2)	52 (48.60%)	18 (23.38%)	3.01	(1.44,6.3)	0.00352
	Grade III (2.5 & 3)	5 (4.67%)	1 (1.30%)	1.66	(0.15,18.57)	0.67904

The combination of GI symptoms, anorexia, disproportionate diet, and anxiety was seen in 30 patients, while 154 lacked the combination. Although the group showed a higher incidence and higher odds ratio with disease severity, CRP elevation, and coated tongue, it could not achieve statistical significance.

Table 7
Combination (GI symptoms, Anorexia, Disproportionate Diet, Anxiety with insomnia)

Parameters		Combination (30)	Non-combination (154)	Odds Ratio	95% CI	p-value
C-REACTIVE PROTIEN	CRP [0-6]	10 (33.33%)	49 (31.82%)	-	-	-
	CRP (>6,30]	7 (23.33%)	63 (40.91%)	0.54	(0.18,1.66)	0.28457
	CRP (30,60]	3 (10.00%)	16 (10.39%)	0.92	(0.2,4.37)	0.92046
	CRP (>60)	6 (20.00%)	16 (10.39%)	1.4	(0.34,5.73)	0.63806
D-DIMER	D-dimer [0-500]	14 (46.67%)	79 (51.30%)	-	-	-
	D-dimer (>500)	9 (30.00%)	53 (34.42%)	0.7	(0.24,2)	0.50074
DISEASE SEVERITY	Mild	11 (36.67%)	91 (59.09%)	-	-	-
	Moderate	14 (46.67%)	51 (33.12%)	1.54	(0.55,4.35)	0.41118
	Severe	2 (6.67%)	9 (5.84%)	1.17	(0.16,8.54)	0.8773
	Critical	3 (10.00%)	3 (1.95%)	1.29	(0.13,13.31)	0.83015
CT-SEVERITY	HRCT - 0	3 (10.00%)	11 (7.14%)	-	-	-
	HRCT - [1,8]	8 (26.67%)	28 (18.18%)	0.61	(0.11,3.57)	0.58606
	HRCT - [9,15]	3 (10.00%)	15 (9.74%)	0.26	(0.03,2.05)	0.20253
	HRCT - [16,25]	5 (16.67%)	8 (5.19%)	0.62	(0.08,4.71)	0.64685
COATED TONGUE SEVERITY	Grade I (0.5 & 1)	9 (30.00%)	76 (49.35%)	-	-	-
	Grade II (1.5 & 2)	15 (50.00%)	55 (35.71%)	2.45	(0.91,6.59)	0.07592
	Grade III (2.5 & 3)	4 (13.33%)	2 (1.30%)	8.03	(0.87,74.52)	0.06669

Outcomes for the secondary objective

The secondary objective to check the effect of diet modified as per principles of jwara, with and without ayurvedic medicines, was evaluated with the help of the following endpoints:

1) Mortality
2) Reduction of CRP after treatment
3) Reduction of D-Dimer after treatment
4) Total steroid requirement
5) Need for oxygen
6) Days taken for functional recovery
7) Need for hospitalization
8) Occurrence of post covid sequelae

The confounding factors considered for regression analysis were overall risk for COVID progression, disease severity, vaccination, remedesivir usage, steroid usage, and dietary compliance.

Effect of Ayurvedic diet on disease outcomes

A total of 120 patients reported good compliance with the ayurvedic diet prescribed, while 64 patients reported an average or poor compliance with the diet. The most remarkable feature seen was the complete absence of mortality in patients with good dietary compliance, as opposed to 12.5 %(n=8) mortality in patients without dietary compliance. Also, the good compliance group took much fewer days to functional recovery as compared to the average and poor compliance group, which had a very high odds ratio of a slower recovery with a significant P-value. The incidence of post covid sequelae is also significantly higher in the average and poor compliance group, as compared to the good compliance group. Although oxygen requirement and hospitalization were much less frequent in the good dietary compliance group, it did not meet statistical significance. CRP and D-dimer reduction, although they showed a good clinical response it could not be demonstrated in view of the variability in timing and limitations of data/sample recording, with some

segments showing a opposite effect, which was never seen clinically. similar was the case with steroid requirement, which could not be demonstrated mathematically, although clinically seen.

Table 8
Effect of Ayurvedic diet

Parameter	Ayurvedic medication (n=139)	No Ayurvedic medication (n=45)	Odds	95% CI	p-value
Mortality					
Recovered	120(100.00%)	55(85.94%)	-	-	-
Death	-	8(12.50%)	4.74×10^{13}	$(0,1.18 \times 10^{308})$	0.92745
Reduction of CRP after treatment					
[-6,6]	44(36.67%)	11(17.19%)	-	-	-
[-60,-30)	-	2(03.13%)	$4.79 \times e^{10}$	$(1.55 \times e^{10}, 1.48 \times e^{10})$	-
[-30,-6)	4(03.33%)	-	0	(0,0)	-
(6,30)	31(25.83%)	9(14.06%)	1.07	(0.36,3.22)	0.89781
[30,60)	5(4.17%)	9(14.06%)	5.39	(1.32,22.1)	0.01924
[60,90)	2(1.67%)	4(6.25%)	3.32	(0.43,25.37)	0.24721
greater than or equal to 90	3(2.50%)	2(03.13%)	0.35	(0.02,5.16)	0.44238
CRP Trend Classification Post Treatment					
Normal	44(36.67%)	11(17.19%)	-	-	-
Elevation	4(03.33%)	2(03.13%)	1.49	(0.19,11.73)	0.70724
Reduction	41(34.17%)	24(37.50%)	1.72	(0.67,4.39)	0.25804
Reduction of D-Dimer after treatment					
[-400,400]	49(40.83%)	13(20.31%)	-	-	-
[-2000,-1000]	1(00.83%)	1(01.56%)	0.43	(0.01,15.93)	0.64509
(-1000,0]	4(03.33%)	3(04.69%)	3.61	(0.62,21.2)	0.155
(0,500]	15(12.50%)	8(12.50%)	1.71	(0.52,5.63)	0.37852
(1000,2000]	6(05.00%)	2(03.13%)	0.79	(0.12,5.32)	0.81084
(500,1000]	7(05.83%)	5(07.81%)	2.48	(0.56,11.03)	0.23201
>2000	1(00.83%)	5(07.81%)	19.18	(1.75,210.06)	0.01556
Total steroid requirement					
less than or equal 40	4(03.33%)	4(06.25%)	-	-	-
[41-80]	3(02.50%)	4(06.25%)	1.71	(0.14,20.59)	0.6734
[81-225]	5(04.17%)	6(09.38%)	0.73	(0.07,7.88)	0.7927
[226-400]	4(03.33%)	4(06.25%)	0.06	(0,2.13)	0.1216
[401-800]	4(03.33%)	4(06.25%)	1.03	(0.07,15.36)	0.9847

[801-2000]	3(02.50%)	4(06.25%)	0.82	(0.03,22.74)	0.9069
Above 2000	1(00.83%)	4(06.25%)	1.64	(0.01,231.16)	0.8446
Need for oxygen					
Oxygen requirement	10(08.33%)	19(29.69%)	1.16	(0.24,5.59)	0.6734
No Oxygen requirement	104(86.67%)	40(62.50%)	-	-	-
Days taken for functional recovery					
Parameter	**Ayurvedic medication (n=139)**	**No Ayurvedic medication (n=45)**	**Odds**	**95% CI**	**p-value**
0-3	31(25.83%)	2(03.13%)	-	-	-
4-7	53(44.17%)	16(25.00%)	4.34	(0.84,22.47)	0.08051
8-14	25(20.83%)	18(28.13%)	7.52	(1.36,41.68)	0.02088
15-30	2(01.67%)	12(18.75%)	43.41	(4.38,430.52)	0.00128
>30	1(00.83%)	2(03.13%)	28.86	(1.01,827.84)	0.04957
Need for hospitalization					
Hospitalization	13(10.83%)	23(35.94%)	1.26	(0.27,5.92)	0.37852
Non-Hospitalization	107(89.17%)	41(64.06%)	-	-	-
Post covid sequelae					
No post covid sequelae	104(86.67%)	39(60.94%)	-	-	-
Post covid sequelae	16(13.33%)	20(31.25%)	3.48	(1.41,8.54)	0.0066

Effect of Ayurvedic medications on disease outcomes

A total of 139 patients used ayurvedic medications for a duration of at least 5 days or more, compared to 45 who did not use ayurvedic medications. Most of the parameters tested demonstrated a significant improvement in outcomes with Ayurvedic medications. The mortality rate was significantly lower in patients using Ayurvedic medications compared to non-users. Patients on ayurvedic medications also showed a statistically significant reduction of CRP. A much lower requirement of oxygen, a lower need for hospitalization, much faster functional recovery, and a lower incidence of post-COVID sequelae compared to non-users. D-dimer and steroid usage did not show a consistent relationship, probably due to limitations in sample collection timing and complexity of real-time situations of initiation of steroids.

Table 9
Effect of Ayurvedic medications

Parameter	**Ayurvedic medication (n=139)**	**No Ayurvedic medication (n=45)**	**Odds**	**95% CI**	**p-value**
Mortality					
Recovered	136 (97.84%)	39 (86.67%)	-	-	-
Death	3 (2.16%)	5 (11.11%)	0.04	(0,0.84)	0.03833
Reduction of CRP after treatment					
[-6,6]	42 (30.22%)	13 (28.89%)	-	-	-
(6,30)	(0.00%)	2 (4.44%)	0	-	-
[-30,-6)	3 (2.16%)	1 (2.22%)	4.7	(0.14,163.17)	0.39246
Parameter	**Ayurvedic medication**	**No Ayurvedic medication**	**Odds**	**95% CI**	**p-value**

	(n=139)	(n=45)			
[-60,-30)	35 (25.18%)	5 (11.11%)	2.24	(0.7,7.22)	0.17618
[30,60)	14 (10.07%)	(0.00%)	13.6 x 10^{10}	(4.32 x 10^{10} ,43.18 x 10^{10})	-
[60,90)	4 (2.88%)	2 (4.44%)	1.26	(0.16,10.16)	0.82661
greter than or equal to 90	5 (3.60%)	(0.00%)	6.27 x 10^{11}	(1.62 x 10^{11},24.17 x 10^{11})	-
CRP Trend Classification Post Treatment					
Normal	42 (30.22%)	13 (28.89%)	-	-	-
Elevation	3 (2.16%)	3 (6.67%)	0.36	(0.04,2.91)	0.33478
Reduction	58 (41.73%)	7 (15.56%)	3.51	(1.17,10.49)	0.02468
Reduction of D-Dimer after treatment					
[-400,400]	50 (35.97%)	12 (26.67%)	-	-	-
[-2000,-1000]	2 (1.44%)	(0.00%)	2.98 e^{+23}	(1.60 e^{+23},5.55 e^{+23})	0
(-1000,0]	6 (4.32%)	1 (2.22%)	1.53	(0.16,14.49)	0.71268
(0,500]	20 (14.39%)	3 (6.67%)	1.77	(0.42,7.34)	0.43434
(500,1000]	10 (7.19%)	2 (4.44%)	1.25	(0.22,7.19)	0.80486
(1000,2000]	7 (5.04%)	1 (2.22%)	1.63	(0.16,17.02)	0.68201
>2000	5 (3.60%)	1 (2.22%)	1.66	(0.16,16.88)	0.66981
Total steroid requirement					
less than or equal 40	8 (5.76%)	1 (2.22%)	-	-	-
[41-80]	6 (4.32%)	1 (2.22%)	1.42	(0.04,49.71)	0.84558
[81-225]	10 (7.19%)	1 (2.22%)	2.62	(0.08,89.14)	0.59250
[226-400]	6 (4.32%)	2 (4.44%)	1.2	(0.03,42.05)	0.91926
[401-800]	3 (2.16%)	5 (11.11%)	0.16	(0.01,4.41)	0.27723
[801-2000]	6 (4.32%)	1 (2.22%)	4.56	(0.05,427.04)	0.51211
Above 2000	2 (1.44%)	3 (6.67%)	0.21	(0.01,6.78)	0.73986
Need for oxygen					
Oxygen	13 (9.35%)	16 (35.56%)	-	-	-
No Oxygen	116 (83.45%)	28 (62.22%)	7.74	(1.35,44.23)	0.02141
Days taken for functional recovery					
0-3	25 (17.99%)	8 (17.78%)	-	-	-
04-7	62 (44.60%)	7 (15.56%)	3.01	(0.88,10.27)	0.07903
8-14	34 (24.46%)	9 (20.00%)	2.02	(0.51,7.96)	0.31599
15-30	10 (7.19%)	4 (8.89%)	1.38	(0.21,9.09)	0.73986
>30	1 (0.72%)	2 (4.44%)	0.03	(0,1.4)	0.07321
Need for hospitalization					
Hospitalization	17 (12.23%)	19 (42.22%)	-	-	-
Non-Hospitalization	122 (87.77%)	26 (57.78%)	15.71	(2.13,115.91)	0.0069
Parameter	**Ayurvedic medication (n=139)**	**No Ayurvedic medication (n=45)**	**Odds**	**95% CI**	**p-value**
Post covid sequelae					
No post covid sequelae	111 (79.86%)	32 (71.11%)	-	-	-
Post covid sequelae	26 (18.71%)	10 (22.22%)	1.02	(0.4,2.64)	0.96482

Combined effect of Diet and medications

A total of 98 patients used ayurvedic medications and showed good compliance with the ayurvedic diet, as opposed to 86 patients who did not use medications and showed average or poor compliance with the diet prescribed. Once again, the combination group with good compliance showed absolutely no mortality when compared to the poor compliance combination group, which had 9.3% mortalit y. The good compliance combination group also showed statistically significantly better outcomes in terms of faster functional recovery, lesser post-covid sequelae, lower rate of hospitalization, lesser requirement of oxygen. Although better CRP reduction was clinically visible, it could not be shown statistically. The d-dimer reduction and reduction in need for steroid were appreciated clinically, but were too complex to be demonstrated in the simple scheme of this study.

Table 10
Combined Effect of medications (>=5 days) & good dietary compliance

Parameter	Ayurvedic medication + Good diet (n=98)	No Ayurvedic medication + Average or poor (n=86)	Odds	95% CI	p-value
Mortality					
Recovered	98 (100.00%)	77 (89.53%)	-	-	-
Death	0.00%	8 (9.30%)	0	(0,0)	0
Reduction of CRP after treatment					
[-6,6]	36 (36.73%)	19 (22.09%)	-	-	-
(6,30)	28 (28.57%)	12 (13.95%)	1.33	(0.51,3.48)	0.55714
[-30,-6)	3 (3.06%)	1 (1.16%)	7.09	(0.21,240.34)	0.27571
[-60,-30)	0.00%	2 (2.33%)	0	(0,0)	0
[30,60)	5 (5.10%)	9 (10.47%)	0.46	(0.12,1.84)	0.27456
[60,90)	2 (2.04%)	4 (4.65%)	0.69	(0.09,5.52)	0.72974
greater than or equal to 90	3 (3.06%)	2 (2.33%)	12.14	(0.41,361.45)	0.1493
CRP Trend Classification Post Treatment					
Parameter	**Ayurvedic medication + Good diet (n=98)**	**No Ayurvedic medication + Average or poor (n=86)**	**Odds**	**95% CI**	**p-value**
Normal	36 (36.73%)	19 (22.09%)	-	-	-
Elevation	3 (3.06%)	3 (3.49%)	0.87	(0.12,6.53)	0.89219
Reduction	38 (38.78%)	27 (31.40%)	1.04	(0.45,2.42)	0.92996
Reduction of D-Dimer after treatment					
[-400,400]	41 (41.84%)	21 (24.42%)	-	-	-
[-2000,-1000]	1 (1.02%)	1 (1.16%)	2.27	(0.06,85.35)	0.65694
(-1000,0]	4 (4.08%)	3 (3.49%)	0.68	(0.13,3.72)	0.66136
(0,500]	14 (14.29%)	9 (10.47%)	0.96	(0.31,2.97)	0.9386
(1000,2000]	6 (6.12%)	2 (2.33%)	2.11	(0.32,14.04)	0.43805
(500,1000]	6 (6.12%)	6 (6.98%)	0.51	(0.12,2.09)	0.34668
>2000	1 (1.02%)	5 (5.81%)	0.13	(0.01,1.29)	0.08132
Total steroid requirement					
less than or equal 40	4 (4.08%)	4 (4.65%)	-	-	-
[41-80]	3 (3.06%)	4 (4.65%)	0.73	(0.05,10.03)	0.81474
[81-225]	4 (4.08%)	7 (8.14%)	1.29	(0.1,15.89)	0.84219
[226-400]	4 (4.08%)	4 (4.65%)	24.2	(0.52,1117.45)	0.10324
[401-800]	1 (1.02%)	7 (8.14%)	0.25	(0.01,6.14)	0.39945

[801-2000]	3 (3.06%)	4 (4.65%)	1.97	(0.06,68)	0.70778
Above 2000	1 (1.02%)	4 (4.65%)	0.98	(0.01,161.12)	0.99509
Need for oxygen					
Oxygen	5 (5.10%)	24 (27.91%)	-	-	-
No Oxygen	87 (88.78%)	57 (66.28%)	3.66	(0.58,23.12)	0.16725
Days taken for functional recovery					
0-3	24 (24.49%)	9 (10.47%)	-	-	-
4-7	49 (50.00%)	20 (23.26%)	1	(0.36,2.77)	0.99292
8-14	20 (20.41%)	23 (26.74%)	0.49	(0.15,1.56)	0.22428
15-30	1 (1.02%)	13 (15.12%)	0.05	(0,0.52)	0.01255
>30	1 (1.02%)	2 (2.33%)	0.11	(0,2.94)	0.18954
Need for hospitalization					
Hospitalization	6 (6.12%)	30 (34.88%)	-	-	-
Non-Hospitalization	92 (93.88%)	56 (65.12%)	10.1	(1.44,71.13)	0.02019
Post covid sequelae					
No post covid sequelae	86 (87.76%)	57 (66.28%)	-	-	-
Post covid sequelae	12 (12.24%)	24 (27.91%)	0.31	(0.13,0.75)	0.00951

3.2 Discussion

While covid-19 pandemic battered countries, and almost whole of the scientific world focused on the "magic pi l", ignoring the possibility of many such pathogens/ mutants that may arise in future, and the futility of the individual pill based approach against this reality this study conducted in resource -limited settings, aims to draw attention of the scientific community to the extremely unique Ayurvedic concept of a dietary role on host-responses, during an acute infectious process like COVID-19 infection, and role of its modification on outcomes. Also, more specifically, it focuses on the contribution of specific dietary items in the pathogenesis of the day-regulated host-immune responses and inflammation. It also attempts to study the importance of simple clinical symptoms and signs like anorexia, nausea, vomiting, and a coated tongue in the management of infections and inflammation.

Summary of key results

Despite a resource crunch, rigorous statistical methods like logistic regression analysis were used to eliminate the effect of various confounding factors, which are inherent when trying to look at novel associations or etiological factors.

A significant part of the results in primary objectives was a very strong statistical correlation between the presence of Gi symptoms and the presence of Anorexia in particular, with the more severe manifestations of the disease, clinically, biochemically, and radiologically; and this correlation was stronger with severe forms of GI symptoms. Although this can be argued as consistent with manifestations of severe disease itself, the next part of the observation showed a statistically significant correlation between intake of a disproportionate diet and incidence of a more severe disease in terms of higher CRP, severe clinical disease, and higher radiological scores, and a simple clinical sign like a coated tongue to predict it. By far the most significant part of the study in terms of the primary objectives was the observation that when a disproportionate diet was combined in a patient with anorexia, it was strongly associated with clinical. Biochemical and radiological markers of severe disease. Although this was clinically associated with anxiety as well, it could not be shown statistically.

In the secondary objectives, use of ayurvedic medications for a duration of at least 5 days and more was associated with better reduction of CRP, sometimes d-dimer, lower requirement for oxygen and hospitalisation, faster recovery, significantly lower mortality rates, and marginally lower incidence of post covid sequelae. But what was really a standout feature was the role of diet modification in recovery. Diet modification alone or in combination with medications resulted in almost complete absence of mortality, a very fast recovery with very few post covid sequelae apart from lower oxygen requirement and hospitalisation. The

biochemical benefit in terms of lowered CRP and d-dimer was not as evident, probably due to the simple scheme of only 2 collection points in a complex disease process.

Limitations of the study

The study had important limitations peculiar to retrospective studies undertaken in a pandemic, in terms of not having systematic periods of observation, particularly in terms of biochemistry and radiology. This was because of the pandemic situation, online mode of consultations sought by the majority of patients, reluctance of patients to get exposed to laboratory personnel or visit labs etc. this limitation was not applicable as much for clinical parameters, as online consultations in fact facilitated a regular observation, so this resulted in clinical and lab parameters not correlating temporally in some patients, as labs would have been done days after a symptoms etc.

Inability to incorporate multiple, temporally distributed and variegated laboratory or clinical observations into a simple scheme of observation/calculation was sought to be mitigated by using ranges, as well as the highest and lowest values or simple groups (although not homogenous) for incorporating them into comparative statistics.

The objectives also involved seemingly very subjective parameters like disproportionate diet or dietary compliance, which were necessitated in view of the parameters set out to be tested. Ayurveda, being a clinical science, necessitates the use of such subjective parameters, resulting in this seeming limitation.

Recall bias was possible in dietary assessments, but was minimized by repeated observations, leading to heightened awareness in patients of its importance.

Also, being done in resource-limited situations and single consultant clinics may add to some limitations, like the inability to add more elaborate subgroup analysis, comparison between different waves of the pandemic, analyzing the effect of individual medications, etc.

Interpretation (in view of overall and other evidence)

The study does seem to suggest that specific dietary items described as 'guru' or 'ati-snigdha' in Ayurveda and clinically interpreted to mean fat-rich, fiber-rich, mucilaginous, uncooked foods in this study, are relevant for the pathogenesis of sars-co-2, may have a causative role in the inflammatory host response as well as hypercoagulability. More specifically, when it is consumed by a person with anorexia, it is thought to represent a generalized sluggishness of metabolism and the digestive system in particular. The mechanism seems plausible, as a gut with sluggish metabolism may find it difficult to digest these foods, which may need an energy-intensive process to complete digestion, absorption, assimilation, and utilization. This may result in partially processed intermediates (called as 'ama' in Ayurveda, meaning unripe/uncooked), which behave as non-self antigens due to their non-assimilation, which may elicit a different kind of host response characterized by inflammation and hypercoagulability in the short run and autoimmunity in the long run (Adluri & Bhattacharya, 2022).

This is also seemingly validated by the results of the secondary objectives, which seem to suggest that elimination of the same items and optimizing diet to be proportionate to one's appetite, and using only simple starches and plant-based protein from green gram or processing it with simple herbs, seems to improve outcomes both in the short term and long term, including a significant reduction in mortality and morbidity. Ayurvedic drugs also seem to augment this process significantly, primarily by their effect on digestive metabolism described as 'deepana and pachana' in Ayurveda, but essentially focused on metabolizing these intermediates called as ama.

Generalizability of the study

Modern medicine is beginning to understand the role of diet in infections, some recent studies have tried to utilizer "hypocaloric" diets in management of acute sepsis, although overa l consensus is yet to emerge (Perman et al., 2018), similar attempts have been made with mediterranean and other 'healthy' diets (Sharma et al., 2023). This study aims to study the role of Ayurvedic diet based on the principles of jwara, both in the causation and the management of acute SARS COV-2 infections. Although done in resource limited setting, it offers an important first step in exploring the role of diet in host response modification in acute infections. The results seem to validate the millennia old concepts of ayurveda in terms of both the causative

and curative aspects of diet in jwara or an acute infectious/inflammatory process.it draws attention to the urgent need for further research and validation that needs to be done in this area. Also, the concept of diet/ nutrition needs to be redefined so as to incorporate concepts like the 'gunas" or qualities described in ayurveda, so that particular items peculiar to different geo-climatic regions and to different races can be evaluated in future studies before generalizing the results of this study.

Also, better quality and randomized -controlled with a more planned study design need to be conducted based on the leads given by this study before its generalization. Exceptions to langhana process described in ayurvedic classics like severe emaciation, children, very elderly or fevers with dominance of vata etc., cannot be generalised to this approach based on the results of this study. And this also explains the major concern against hypocaloric diets, by using a balanced approach, wherein the nutritional needs of the patient are to be balanced against his/her ability to digest, metabolize and utilize them, any fasting or calorie restriction cannot be to a degree that compromises the strength of the patient and endangers life (Sharma, 2011).

4 Conclusion

Although done in a single center, this study based on ayurvedic understanding of jwara, takes an alternative route to face the challenge of new and emerging infections/pandemics, by focusing on the possible role of diet in eliciting particular kind of host responses like inflammation or hyper coagulability, particularly when associated with reduced appetite and the role of diet modifica t ion to reverse the pathology and thus limit mortality and morbidity. Prima facie, it supports the conclusion of a dietary role in pathogenesis and management. It also supports the role of Ayurvedic medicines and medicated water in the management of the same. It flags the importance of symptoms like anorexia or signs like a coated tongue, while deciding the nutrition of a patient. Further, more planned studies are needed to validate this approach and bring it into the mainstream of global management of inflammations/infections, and lessen the focus on an anti-microbial-based approach.

Peculiarities- particular diet as cause of inflammation, mechanism of inflammatory response(ama), importance of appetite in deciding nutrition, appetite as a general marker of overall metabolism, diet as a means to modulate host response, alternative approaches to infection control/seps is prevention/ antimicrobial approach. New pandemic preparedness. novel etiologies in inflammatory/auto- immune diseases,

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Authorship Contribution
The author contributed significantly to the conception, design, data acquisition, analysis, and interpretation of the work. Authors were involved in drafting and revising the manuscript, and approved the final version for publicationn.

Icmje Statement
We have met the criteria recommended by the International Committee of Medical Journal Editors (ICMJE) for authorship and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Statement
This study was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. Formal approval was obtained from the institutional ethics committee prior to commencement of the study.

Patient Consent
Written informed consent was obtained from all participants included in the study. Confidentiality and privacy of participant information were maintained throughout the research process.

Conflict Of Interest Statement
The authors declare that there are no conflicts of interest related to this study.

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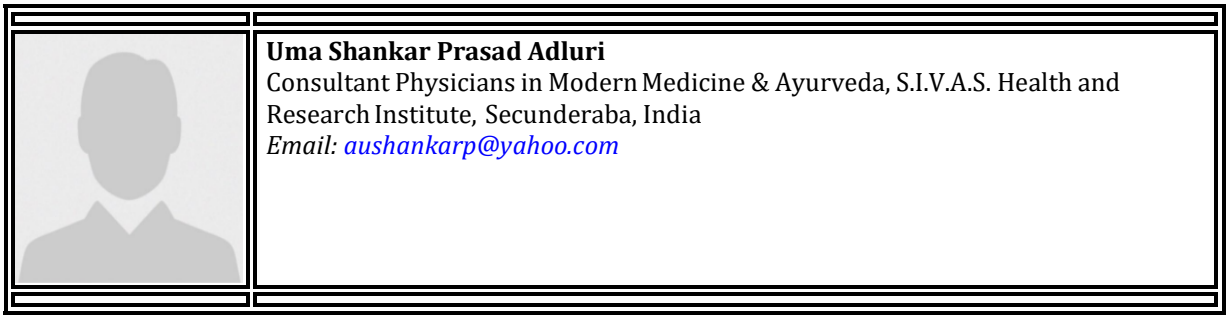
Biography of the Author



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