Journal of Ayurveda and Integrative Medicine 16 (2025) 101045

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: elsevier.com/locate/jaim

Original Research Article

Efficacy of Ayurvedic treatment given to cancer patients in the prevention of COVID-19 – A Retrospective Cohort Study at Integrated Cancer Treatment and Research Centre, Wagholi

Sadanand Sardeshmukh, Vineeta Deshmukh *, Vidya Gupta, Vasanti Godse, Shweta Gujar, Swapna Kulkarni, Sneha Dalvi, Nilambari Sardeshmukh, Bhagyashree Sardeshmukh, Sushama Bhuvad, Sandeep Chavan, Vinita Awalkanthe, Shrinivas Datar, Anita Shingte, Abhishek Salunkhe, Amruta Salunkhe, Sneha Nabar, Dhananjay Deshpande, Trupti Dafare

Bharatiya Sanskriti Darshan Trust's Integrated Cancer Treatment and Research Centre, Wagholi, Pune, Maharashtra, India

ARTICLE INFO

Keywords:
Ayurveda
Cancer
COVID-19
Prevention

ABSTRACT

Background: Cancer patients are considered to have a higher risk of developing severe Coronavirus Disease 2019 (COVID-19) and a higher mortality rate. Moreover, poor prognosis observed in them is associated with multiple co-morbidities. Ayurveda can prove to be effective in preventing COVID-19 as well as improving clinical outcomes against COVID-19 in cancer patients.

Objectives: To evaluate the effect of Ayurvedic treatments given to cancer patients as also a preventive modality against COVID-19 infections.

Methods: 700 cancer patients were enrolled in the study. The demographic information regarding their age, sex, organs involved, stage, pre-existing comorbidities, Karnofsky score, addictions, undergoing conventional cancer treatment, type of conventional treatment, and duration of Ayurvedic cancer treatment was collected from the institutional records. These patients were interviewed telephonically or in person to obtain information related to their COVID-19 status from March 2020 to Sep 2021, which included a) whether they were affected with COVID-19 or not, b) If affected, the severity of COVID-19 symptoms, c) vaccination status, d) mortality, and e) if in contact with relative affected by COVID-19.

Results: The surveyed cohort had 56 years as the median age, more female patients, Karnofsky score between 80 and 100, and hypertension as well as diabetes as major co-morbidities. During the 1st and 2nd waves, 34 (4.85%) and 65 patients (10.09 %) were COVID-19 positive while 4.91 % and 11.11% of patients with addictions were covid positive, respectively, the rest remained unaffected.

There was no specific trend in % of COVID-19-positive cancer patients concerning stage, but those with stage IV undergoing conventional treatment showed increased prevalence ($p < 0.001$). Prolonged Ayurvedic treatment exhibited a decreasing trend in % COVID-19 positive patients, which is highly significant ($p < 0.001$). Specifically, those undergoing conventional therapy, and also received Ayurvedic treatment simultaneously for more than 3 years remained unaffected by COVID-19, which was statistically significant in both waves ($p < 0.001$).

Conclusion: Ayurvedic treatments given to cancer patients are effective in preventing COVID-19 infections in these patients.

1. Introduction

Coronaviruses belong to the family of viruses that are responsible for a wide range of respiratory diseases ranging from mild cold to severe distress. In December 2019, coronavirus named SARS-CoV- 2 resulted in an outbreak of COVID-19 [1]. India has recorded over 4.44 crore

Peer review under responsibility of Transdisciplinary University, Bangalore.

* Corresponding author. Bharatiya Sanskriti Darshan Trust's Integrated Cancer Treatment and Research Centre, Kesnand Road, Wagholi, Pune, 412207, Maharashtra, India.

E-mail address: ictrcpune@gmail.com (V. Deshmukh).

https://doi.org/10.1016/j.jaim.2024.101045

Received 31 July 2023; Received in revised form 5 August 2024; Accepted 5 August 2024

COVID-19 cases and 5.31 lacs deaths since the outbreak to date [2]. The majority of the cases with SARS-CoV-2 infections were either asymptomatic or developed a mild illness (which included fever, cough, briefness of breath, and muscle pain), while some required hospitalization and oxygen support (which included acute respiratory torture pattern [3] acute renal failure, acute respiratory injury, septic shock, and severe pneumonia), and few were admitted to an intensive care unit (ICU) [4].

SARS-CoV-2 infection and COVID-19 can affect anyone, although the risk of developing a serious sickness rises with age and presence of certain underlying medical disorders, such as cancer. Due to the illness itself and/or the cancer treatment such as surgery, radiotherapy, and chemotherapy, patients with active cancer are typically more vulnerable to infections. As reported previously [5], cancer patients are more likely to develop serious infections and to require mechanical breathing or admission to the ICU leading to death. An increased risk of severe infection and COVID-19-specific death in cancer cases was linked to the male gender, Asian race, haematological cancer, first 24 months since cancer diagnosis, fever, dyspnoea, and particularly high range of ferritin, as well as *C*-Reactive Protein. Additionally, it was established that a history of cancer offered a higher risk for serious complications and was linked to more serious outcomes concerning COVID-19 [1] Furthermore, those over the age of 60 were at a higher risk of COVID-19-related death [6]. A small study of 105 patients reported that lung cancer, metastatic illness, and hematologic malignancy may be associated with greater rates of COVID-19-related death and ICU hospitalization [7].

Despite global efforts to contain it, the pandemic spread due to a lack of scientifically validated preventive and therapy plans. In such a situation, the scientific community pondered upon the pluralistic knowledge systems that are available globally. In this pandemic crisis, China adopted an integrative strategy using Traditional Chinese Medicines (TCM) with modern treatment for more positive results [8]. Similarly, centuries-old Ayurveda medicine was being researched in India for its preventative and curative effects for dealing with COVID-19. According to Ayurvedic principles, the COVID-19 pandemic/infection has been linked to *Janapadodhvansa Vyadhi* (Epidemic). *Panchavidha Karma*, viz., *Vamana* (Emesis), *Virechana* (Purgation), *Basti* (Drug enema), *Nasya* (Errhine), and *Raktamokshana* (Bloodletting), have been recommended in the treatment of epidemics but seemed to be overlooked during the widespread of COVID-19 [9] *Rasayana,* another unique Ayurvedic concept associated with immunomodulation is also indicated, which surely has a key role in COVID-19 [10].

The current study intends to evaluate the effect of Ayurvedic treatments, particularly *Rasayana* and *Panchakarma,* given to cancer patients to improve their Quality of Life and control cancer recurrence/metastasis, which could prove as a preventive modality against COVID-19 infections. No specific interventions were done for COVID 19 though.

2. Methods

2.1. Study design

This is a monocentric observational cohort study designed to determine the efficacy of Ayurvedic cancer treatment in the prevention of COVID-19. It was conducted in December 2020 and December 2021, with a primary focus on COVID-19 Wave 1 (Mar to Oct 2020) and Wave 2 (Mar to Sep 2021) in the Indian scenario [11]. This study was carried out as per the Declaration of Helsinki following STROBE guidelines [12], Cancer patients were treated for cancer with various combinations of Ayurvedic formulations possessing *Shamana* (*Dosha* and *Dhatu* balancing treatment) and *Rasayana* properties as listed in Supplementary File 1 along with conventional cancer treatment. Some of them were treated with *Panchakarma* (detoxifying) therapies as well. No specific intervention for COVID-19 was done [13]. The Institutional Ethics Committee was informed about this observational study. No CTRI registration was done since, it was an observational study, with no intervention for COVID-19 was done.

2.2. Participants

Participants' written and informed consent was taken at the time of registration at our center. Cancer patients registered at our institute from 1996 to 2020, irrespective of the type, stage, and grade of cancer, with ongoing Ayurvedic treatment (for 1996 to 2019 registered patients) or those who have received Ayurvedic treatment for at least six months (for 2020 registered patients) were included in the study.

Effect of Ayurvedic treatment in the form of improvement in Quality of Life and immunomodulation is observed in cancer patients when they are regularly taking Ayurvedic treatment at least for 6 months. For this purpose, patients who had discontinued the treatment and were not under regular follow-up or those who received treatment for less than 6 months were excluded from the study. The formal sample size calculation was later performed at a 95% confidence level and $\pm$ 0.5% confidence interval, with a standard deviation of 0.5 for about 900 eligible cancer patients treated at our institute. The minimum sample size equivalent to representing this population was only 270 and we surveyed a total of 700 patients (Fig. 1).

2.3. Outcomes

The study's primary outcome was the proportion of cancer patients affected by COVID-19, the severity of COVID-19 in cancer patients, the types of conventional treatments administered for COVID-19 in cancer patients, and the mortality rate among cancer patients with COVID-19. Ongoing conventional treatment and close contact with infected relatives were factors of interest (exposures). The organs affected by cancer, type of cancer, cancer treatment status, type, and duration of Ayurvedic treatment were used to predict the study outcomes. Patient's overall health status assessed by Karnofsky score (KPS), age, comorbidity, addiction, ongoing conventional treatment, and access to health care could potentially influence the outcomes or exposures. In this study, potential effect modifiers including the vaccination status, duration, and type of Ayurvedic treatment received could impact COVID-19 outcomes differently for diverse cancer types or stages.

2.4. Data collection

Demographic features, pre-existing comorbidities, addiction status, histopathological confirmation of cancer diagnosis, and staging were extracted from patient records. The COVID-19 status i.e., positive RT-PCR status was ascertained through in-person or telephonic interviews conducted by a team of doctors and trained Medical Social Workers (MSWs) at the institute. Data included information related to COVID-19 disease, contact history, symptom onset and duration, medication use, and adverse reactions. Vaccination data, including vaccine type and dosing dates, were recorded. Family members' COVID-19 infection status and well-being during both waves were also included.

2.5. Risk of bias

To prevent information bias, a self-explanatory and user-friendly questionnaire (Supplementary file 2) incorporating all the above-mentioned aspects of the study was designed and we ensured that the data were collected only by qualified doctors and trained MSWs. We have included cancer patients of all types, stages, and grades in the study to ensure unbiased selection.

2.6. Statistics

For this investigation, formal sample size calculation was later performed as given in 2.2. In a Microsoft Excel file (Microsoft Office version

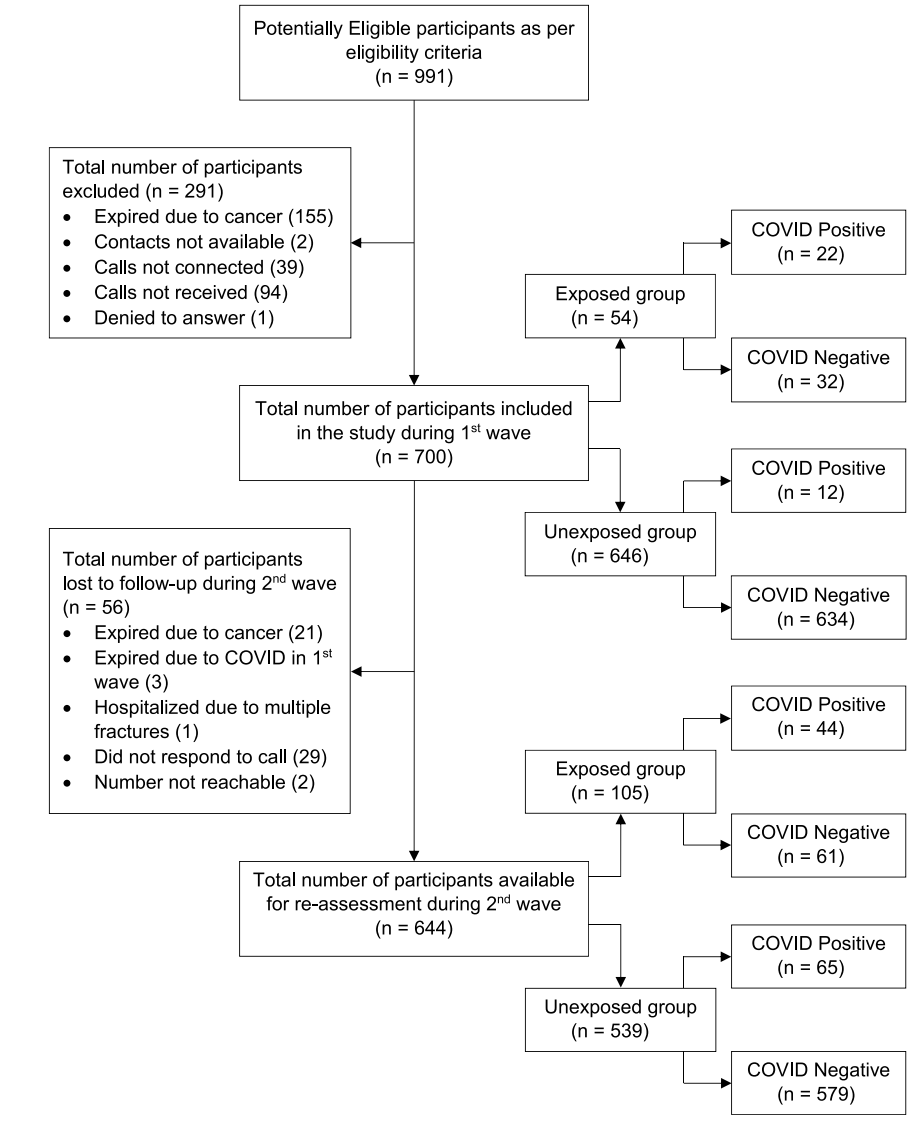

Fig. 1. Flow chart depicting the screening process of the participants.

2010), patients were assigned a unique recognition code. The non-parametric 'Chi-square' test was applied for statistical analysis as data was categorial and had a relatively large sample size. Statistical significance was set at a *p*-value of 0.05 on both sides. After completion of the study post hoc analysis was performed to understand the power of the study. Power analysis was established by G*Power 3.1.9.4 (Franz Faul Universität, Kiel Germany) [14].

3. Results

During the 1st Wave (Mar to Oct 2020), 700 patients were interviewed about their COVID-19 status while during the 2nd Wave (Mar to Sep 2021), 644 of these patients were available for re-evaluation as 56 patients were lost to follow-up in the 2nd wave. The power achieved for the test is about 0.99 (99%) for a sample size of 700 and a level of significance of 0.05 (5%). The screening process has been detailed in Fig. 1.

During the 1st and 2nd waves, 34 (4.85%) and 65 (10.09 %) patients, respectively were COVID-19 positive (Table 1). Categorization of the COVID-19-positive patients into symptomatic/asymptomatic groups and various classes of severity, with or without vaccination has been depicted in Table 1. It was found that the number of COVID-19 symptomatic patients increased during the second wave (n = 54, 83.08%) as compared to the 1st wave (n = 24, 70.58%) (Table 1).

The proportion of females (53 and 61.5 % during the 1st and 2nd waves, respectively) was higher than that of males. Most of the patients had Karnofsky's score of 80 in the first wave (1.86%), while 3.88% had scores of 90 in the second wave. In both waves, the most frequent signs and symptoms were fever, breathlessness, cold, and cough. Also, in the second wave, more patients presented with loss of smell, loss of taste, and weakness, as compared to the gastrointestinal symptoms (Table 1). On evaluating the differences in treatments during both waves, a maximum number of patients were home quarantined during the second wave (64.61%) than in the first wave (32.35%). Subjects from the second wave were treated more often with hospitalization, conventional oxygen therapy, and Remdesivir and less often with invasive mechanical ventilation. The rate of mortality among cancer patients in this cohort was reduced by 50% during the second wave (Table 1). In patients having addictions, only 4.91?? and 11.11% were COVID-19 positive in the 1st and 2nd wave, respectively (Table 1). Notably, 95.2?? and 89.9% of patients who received either *Shamana, Rasayana,* or *Shamana,*

Table 1
Distribution of cancer patients analyzed during 1st and 2nd wave of COVID-19 pandemic.

Criteria	No. of Patients In 1st Wave (%) (n = 700)		No. of Patients In 2nd Wave (%) (n = 644)	
COVID Status	COVID + ve	COVID -ve	COVID + ve	COVID -ve
	34 (4.90)	666 (95.1)	65 (10.1)	579 (89.9)
Sex				
Male	16 (47)	218 (32.7)	25 (38.5)	182 (31.4)
Female	18 (53)	448 (67.3)	40 (61.5)	397 (68.5)
Vaccination Done				
Yes	25 (73.5)	536 (80.5)	56 (86.2)	470 (81.2)
No	09 (26.5)	130 (19.5)	09 (13.8)	109 (18.8)
Karnofsky Performance Score				
50	0	02 (0.3)	0	15 (03)
60	02 (06)	06 (01)	04 (06)	13 (02)
70	03 (09)	48 (07)	09 (14)	35 (06)
80	13 (38)	172 (26)	12 (18)	145 (25)
90	11 (32)	265 (40)	25 (38)	216 (37)
100	05 (15)	173 (26)	15 (23)	155 (27)
Addictions				
Yes	17 (50)	329 (49.4)	35 (53.8)	280 (48.4)
No	17 (50)	337 (50.6)	30 (46.2)	299 (51.6)
Presentation				
Asymptomatic	10 (29.42)	–	11 (16.92)	–
Symptomatic	24 (70.58)		54 (83.08)	
Presenting Symptoms				
Fever	19 (79.16)	–	41 (75.92)	–
Headache	04 (16.67)		02 (03.70)	
Breathlessness	05 (20.83)		10 (18.50)	
Weakness	05 (20.83)		15 (27.78)	
Cough and Cold	09 (37.50)		29 (53.70)	
Body ache	04 (16.67)		11 (20.37)	
Anorexia	04 (16.67)		07 (12.96)	
Loss of Taste	07 (29.16)		14 (25.92)	
Loss of Smell	04 (16.67)		17 (31.48)	
Insomnia	00		01 (01.85)	
Diarrhoea	00		01 (01.85)	
Severity of COVID-19-Positive Patients and Modern Treatment Received				
Home Quarantine	11 (32.35)		42 (64.61)	
Hospitalized	19 (55.58)		22 (33.34)	
Hospitalized and on O2	0		4 (6.15)	
Hospitalized and treated with Remdesivir	4 (11.76)		3 (4.61)	
Hospitalized and on O2 + Remdesivir	1 (2.94)		8 (12.30)	
Hospitalized and on ventilators	4 (11.76)		1 (1.54)	
Expired	6 (17.65)		3 (4.61)	
Ayurvedic Treatment Received				
Shamana + Rasayana	23 (67.6)	449 (67.4)	38 (58.45)	395 (68.21)
Shamana + Rasayana + Panchakarma	11(32.3)	216 (32.45)	27 (41.55)	183 (31.6)

Rasayana, and *Panchakarma* were COVID-19 negative in the 1st and 2nd wave, respectively (Table 1). The age-wise distribution of COVID-19-positive and negative patients has been depicted in Table 2. The median age was 56 years (50–62 years). No significant difference in age distribution was observed between the COVID-19 positive and negative patients in both waves.

A significantly higher ($p < 0.0001$) number of patients were of breast cancer (32% in both waves), hemopoietic (17.65% in 1st wave and 24.62% in 2nd wave), and gastrointestinal cancer (11.76% in 1st wave and 20% in 2nd wave), while lung cancer was mere 5.88% in 1st and none in 2nd wave (Table 3). It was found that though 54 and 104 relatives were COVID-19-positive in the 1st and 2nd waves, respectively, the significant number of cancer patients who remained unaffected were 59.26% (n = 32) and 57.69% (n = 60), respectively in both waves. 22.7 and 23.1% of patients were under conventional cancer treatment during 1st and 2nd wave, respectively; and the majority of them, 94.97 and 87.92%, respectively were COVID-19 negative. This was highly significant ($p < 0.0001$) (Table 3).

There was no specific trend observed in the percentage of COVID-19-positive patients concerning the stage. However, amongst stage IV patients undergoing conventional treatment, the proportion of COVID-19-negative patients (92.86% in 1st wave and 86.27% in 2nd wave) was significantly higher than the proportion of COVID-19-positive patients (7.14% in 1st wave and 13.73% in 2nd wave) (Table 4). Duration of Ayurvedic treatment exhibited a decreasing trend in % COVID-19-positive patients. Cancer patients under conventional therapy, who simultaneously received Ayurvedic treatment for more than 5 years continuously remained unaffected by COVID-19, which was statistically significant ($p < 0.0001$ and $p = 0.0011$ in respective waves) (Table 5a). The majority of the patients received *Basti* treatment (n = 222) followed by *Nasya* (n = 85) and the maximum duration of *Basti* and *Nasya* treatments were 14 and 7 days respectively (Table 5b).

The most prevalent comorbidities were hypertension and diabetes (Table 6). More patients with hypertension and diabetes were affected by COVID-19 during the second wave as compared to the first wave. It was observed that 95.87 and 83.91% of cancer patients having more than two comorbidities were COVID-19 negative in the 1st wave and 2nd wave, respectively; which was a highly significant finding ($p < 0.0001$). Amongst the patients under conventional therapy for cancer, a significant proportion ($p < 0.0001$) i.e., 96.97 and 80% of patients, with more than two comorbidities was COVID-19 negative in respective waves (Table 6).

Table 7 presents that 92.37% of non-vaccinated patients were COVID-19 negative, which was highly significant ($p < 0.0001$). Also, 88.64% of non-vaccinated cancer patients, who were under conventional therapy, remained COVID-19-negative during the second wave.

4. Discussion

We believe that this is the first of its kind report highlighting the efficacy of Ayurvedic treatment given to cancer patients' population in prevention and better prognosis of COVID-19 infection, including those with active cancer disease. Cancer patients treated with adjunct Ayurvedic treatment at our center were selected for this retrospective observational study to assess the incidence rate of COVID-19 among them.

Table 2
Age-wise distribution of cancer patients analyzed during 1st and 2nd wave of COVID-19 pandemic.

1st wave								
Age group (in years)	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square test
		(n)	% (Within Positive patients)	% (Within age group)	(n)	% (Within negative patients)	% (Within age group)	
0–18	9	1	2.94	11.11	8	1.20	88.89	0.0000
19–40	79	5	14.71	6.33	74	11.11	93.67	0.0000
41–60	336	15	44.12	4.46	321	48.20	95.54	0.0000
> 60	276	13	38.24	4.71	263	39.49	95.29	0.0000
Total	**700**	**34**	**100.00**	**4.86**	**666**	**100.00**	**95.14**	0.0000
2nd wave								
Age group (in years)	No. of patients assessed	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test
		(n)	% (Within Positive patients)	% (Within age group)	(n)	% (Within negative patients)	% (Within age group)	
0–18	8	0	0.00	0.00	8	1.38	100.00	0.0000
19–40	74	9	13.85	12.16	65	11.23	87.84	0.0000
41–60	310	31	47.69	10.00	279	48.19	90.00	0.0000
> 60	252	25	38.46	9.92	227	39.21	90.08	0.0000
Total	644	65	100.00	10.09	579	100.00	89.91	0.0000

4.1. Efficacy of Ayurvedic treatment in preventing menace of Covid-19 infection in cancer patients

4.1.1. Association of various risk factors with Covid-19 outcomes

Few reported studies have established an association of variables with COVID-19 outcomes. A study of 193 patients revealed that older age and male gender were associated with a higher likelihood of covid related death, whereas, comorbidities resulted in severe covid 19 symptoms [15]. In this study, it was also observed that treatment with chemotherapy for 90 days before COVID-19 was not associated with COVID-related death and severity. Another study on 112 patients in the Danish cohort also stated that age, performance status, and comorbidities were strong predictors of adverse outcomes in cancer patients with COVID-19 disease. The study also documented that the patients with progressive cancer disease seemed to be at greater risk of fatal outcomes from COVID-19. However, recent cytotoxic therapy was not associated with adverse outcomes of SARS-CoV-2 infection for patients with solid cancer [16]Another study of 198 patients established that factors associated with death after COVID-19 diagnosis were age ≥60 years, current or former smoking, coexisting comorbidities, respiratory tract cancer, and management in a noncurative setting [17] A publication compiling 15 studies with 3019 patients was carried out in the United Kingdom and Europe (41%), followed by the United States and Canada (35.7%), and Asia (China, 23.3%). The overall case fatality rate of COVID-19 patients with cancer measured 22.4%. COVID-19 patients with cancer had a higher fatality rate compared with that of COVID-19 patients without cancer. Age and sex appeared to be the risk factors associated with a poorer prognosis [18] In a study published in The Lancet, 800 cancer patients were studied, 412 (52%) among them had a mild COVID-19 disease course while 226 (28%) patients died. The risk of death was significantly associated with advancing patient age, being male, and the presence of other comorbidities such as hypertension and CVD. These patients had received cytotoxic chemotherapy within 4 weeks before testing positive for COVID-19 [19] Another study carried out on 928 cancer patients in USA, Canada, and Spain documented independent factors associated with increased 30-day mortality, after partial adjustment. They were increased age, male sex, 1 or more comorbidities, Eastern Cooperative Oncology Group performance status of 2 or higher, smoking status, active cancer, receipt of azithromycin plus hydroxychloroquine. Race and ethnicity, obesity status, cancer type, type of anticancer therapy, and recent surgery were not associated with mortality [20]. In another study, out of 423 cancer patients, 40% were hospitalized for COVID-19, 20% developed severe respiratory illness (including 9% who required mechanical ventilation) and 12% died within 30 days. Age older than 65 years and treatment with immune checkpoint inhibitors (ICIs) were predictors for hospitalization and severe disease, whereas receipt of chemotherapy and major surgery were not. Overall, study showed that substantial rates of hospitalization and severe outcomes marked COVID-19 in patients with cancer [21] A study on 212 cancer patients demonstrated a 30% mortality rate. Patients with gastrointestinal cancers were identified as a subset of more vulnerable patients; immunotherapy and radiotherapy within 3 months of COVID-19 diagnosis were risk factors for death [22]. Among 23,266 participants with cancer and 1,784,293 without cancer, 10,404 reported a positive COVID-19 test. It was found that current treatment with chemotherapy or immunotherapy was associated with a 2.2-fold increased risk of a positive test. The association between cancer and COVID-19 infection was stronger among participants >65 years and males [23].

4.1.2. Better outcomes of Ayurvedic treatment in cancer patients associated with various risk factors

Out of 700 cancer patients who were interviewed in the 1st wave, 644 were accessible for reassessment during the 2nd wave. All these patients received Ayurvedic treatment in various combinations of *Shaman*, *Rasayana,* and *Panchakarma* therapies as needed for their ailment for variable periods. In this study, a significantly low prevalence of COVID-19 disease in cancer patients during 1st [n = 34, 4.85%] and 2nd [n = 64, 10.09%)] waves, respectively; can be attributed to their exposure to Ayurveda treatment. Despite the aggressive nature of the disease, being in close contact with COVID-19-positive patients, the presence of comorbidities and addictions, as well ongoing conventional cancer treatment, these immunocompromised cancer patients, who were taking Ayurvedic medicines or had received Ayurvedic treatment previously for a longer duration, showed low susceptibility to COVID-19 as well as less severity, such as hospitalization and mortality rates.

A multicentric cohort study from China reported that breast, colorectal, and lung cancer individuals were the three most prevalent having COVID-19 disease [24]. According to another multivariate analytical study, cancer patients with hematologic malignancy have a worse prognosis during COVID-19 infestation [25]. In our study, it was observed that the occurrence rate of COVID-19 infection was significantly high amongst patients with breast cancer followed by haematological, and gastrointestinal malignancies.

Elderly people having additional illnesses such as comorbidities and concurrent conditions such as obesity, metabolic disorders, lung disease, coronary heart disease, renal failure, fatty liver, and neoplastic disorders are more likely to develop significant COVID-19 infection and face its ill

Table 3
Organ-wise distribution of cancer patients analyzed during 1st and 2nd wave of the COVID-19 pandemic.

Organ	1st wave								2nd wave							
	No of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test
		(n)	% (Within Positive pts)	% (Within CA site)	(n)	% (Within negative pts)	% (Within CA site)			(n)	% (Within Positive pts)	% (Within CA site)	(n)	% (Within negative pts)	% (Within CA site)	
Head and Neck Cancers	86	1	2.94	1.16	85	12.76	98.84	0.0000	78	5	7.69	6.41	73	12.61	93.59	0.0000
GI Track	78	4	11.76	5.13	74	11.11	94.87	0.0000	67	13	20.00	19.40	54	9.33	80.60	0.0000
Respiratory	23	2	5.88	8.70	21	3.15	91.30	0.0000	22	0	0.00	0.00	22	3.80	100.00	0.0000
Sarcomas	18	0	0.00	0.00	18	2.70	100.00	0.0109	16	0	0.00	0.00	16	2.76	100.00	0.0000
Basal Cell Carcinoma	1	0	0.00	0.00	1	0.15	100.00	0.0917	1	0	0.00	0.00	1	0.17	100.00	0.1620
Breast	269	11	32.35	4.09	258	38.74	95.91	0.0000	251	21	32.31	8.37	230	39.72	91.63	0.0000
Female reproductive system	74	1	2.94	1.35	73	10.96	98.65	0.0000	69	6	9.23	8.70	63	10.88	91.30	0.0000
Male reproductive system	18	2	5.88	11.11	16	2.40	88.89	0.0000	17	1	1.54	5.88	16	2.76	94.12	0.0000
Urinary system	10	2	5.88	20.00	8	1.20	40	0.0000	8	1	1.54	12.50	7	1.21	87.50	0.0000
Eye and Brain	13	2	5.88	15.38	11	1.65	84.62	0.0000	13	2	3.08	15.38	11	1.90	84.62	0.0000
Glands (Thyroid & Thymus)	6	1	2.94	16.67	5	0.75	83.33	0.0058	5	0	0.00	0.00	5	0.86	100.00	0.0041
Secondary sites	2	1	2.94	50.00	1	0.15	50.00	0.4187	2	0	0.00	0.00	2	0.35	100.00	0.0112
Hematological	86	6	17.65	6.98	80	12.01	93.02	0.0319	79	16	24.62	20.25	63	10.88	79.75	0.0112
Primary Multiple CA	16	1	2.94	6.25	15	2.25	93.75	0.0000	16	0	0.00	0.00	16	2.76	100.00	0.0000
Total	700	34	100.00	4.86	666	100.00	95.14	0.0000	644	65	100.00	10.09	579	100.00	89.91	0.0000
Cancer patients in contact with COVID-19 positive Relative									104	44	100.00	42.31	60	100.00	57.69	0.0281
Cancer patients undergoing conventional therapy	159	8	100.00	5.03	151	100.00	94.97	0.0000	149	18	100.00	12.08	131	100.00	87.92	0.0000

Table 4
Stage-wise distribution of cancer patients analyzed during 1st and 2nd wave of the COVID-19 pandemic.

Stage of Disease	1st wave								2nd wave							
	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi Square Test	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Value
		(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
I	86	1	2.94	1.16	85	12.76	98.84	0.00	82	10	15.38	12.20	72	12.44	87.80	0.00
II	236	10	29.41	4.24	226	33.93	95.76	0.00	220	21	32.31	9.55	199	34.37	90.45	0.00
III	182	9	26.47	4.95	173	25.98	95.05	0.00	171	13	20.00	7.60	158	27.29	92.40	0.00
IV	149	9	26.47	6.04	140	21.02	93.96	0.00	129	14	21.54	10.85	115	19.86	89.15	0.00
NA	47	5	14.71	10.64	42	6.31	89.36		42	7	10.77	16.67	35	6.04	83.33	
Total	700	34	100.00	4.86	666	100.00	95.14	0.00	644	65	100.00	10.09	579	100.00	89.91	0.00

Cancer patients with COVID-19 negative though relative COVID-19 positive

Stage of Disease	1st wave								2nd wave							
	COVID-19 positive relatives (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test	COVID-19 positive relatives (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square
		(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
I	4	0	0.00	0.00	4	12.50	100.00	0.0019	18	8	18.18	44.44	10	16.67	55.56	0.3152
II	17	7	31.82	41.18	10	31.25	58.82	0.1781	40	17	38.64	42.50	23	38.33	57.50	0.0716
III	16	6	27.27	37.50	10	31.25	62.50	0.0815	21	5	11.36	23.81	16	26.67	76.19	0.0002
IV	11	8	36.36	72.73	3	9.38	27.27	0.0091	16	9	20.45	56.25	7	11.67	43.75	0.1982
NA	6	1	4.55	16.67	5	15.63	83.33	0.0095	9	5	11.36	55.56	4	6.67	44.44	0.2981
Total	54	22	100.00	40.74	32	100.00	59.26	0.0319	104	44	100.00	42.31	60	100.00	57.69	0.0101

Cancer patients undergoing conventional therapy

Stage of Disease	1st wave								2nd wave							
	Patients undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test	Patients undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square
		(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
I	16	0	0.00	0.00	16	10.60	100.00	0.0000	16	0	0.00	0.00	16	12.21	100.00	0.0000
II	35	0	0.00	0.00	35	23.18	100.00	0.0000	32	6	33.33	18.75	26	19.85	81.25	0.0000
III	41	1	12.50	2.44	40	26.49	97.56	0.0000	39	3	16.67	7.69	36	27.48	92.31	0.0000
IV	56	4	50.00	7.14	52	34.44	92.86	0.0000	51	7	38.89	13.73	44	33.59	86.27	0.0000
NA	11	3	37.50	27.27	8	5.30	72.73	0.0127	11	2	11.11	18.18	9	6.87	81.82	0.0001
Total	159	8	100.00	5.03	151	100.00	94.97	0.0000	149	18	100.00	12.08	131	100.00	87.92	0.0000

Table 5a
Duration of Ayurvedic treatment in cancer patients analyzed during 1st and 2nd wave of COVID-19 pandemic.

Duration of Ayurvedic treatment	1st wave								2nd wave							
	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi Square Test	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test
		(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
< 3 y	520	24	70.59	4.62	496	74.47	95.38	0.0000	470	42	64.62	8.94	428	73.92	91.06	0.0000
3–5 y	92	6	17.65	6.52	86	12.91	93.48	0.0000	87	9	13.85	10.34	78	13.47	89.66	0.0000
> 5 y	88	4	11.76	4.55	84	12.61	95.45	0.0000	87	14	21.54	16.09	73	12.61	83.91	0.0000
Total	700	34	100.00	4.86	666	100.00	95.14	0.0000	644	65	100.00	10.09	579	100.00	89.91	0.0000

Cancer patients COVID-19 negative though relative COVID-19 Positive

Duration of Ayurvedic treatment	1st wave								2nd wave							
	COVID-19 positive relatives (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test	COVID-19 positive relatives (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test
		(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
< 3 y	39	16	72.73	41.03	23	71.88	58.97	0.0010	64	26	59.09	40.63	38	63.33	59.38	0.0129
3–5 y	8	3	13.64	37.50	5	15.63	62.50	0.1602	19	9	20.45	47.37	10	16.67	52.63	0.4102
> 5 y	7	3	13.64	42.86	4	12.50	57.14	0.3127	21	9	20.45	42.86	12	20.00	57.14	0.1692
Total	54	22	100.00	40.74	32	100.00	59.26	0.0251	104	44	100.00	42.31	60	100.00	57.69	0.0142

Cancer patients undergoing conventional cancer therapy

Duration of Ayurvedic treatment	1st wave								2nd wave							
	Patients undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test	Pts undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square Test
		(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
< 3 y	146	8	100.00	5.48	138	91.39	94.52	0.0000	137	16	88.89	11.68	121	92.37	88.32	0.0000
3–5 y	3	0	0.00	0.00	3	1.99	100.00	0.0078	4	1	5.56	25.00	3	2.29	75.00	0.0716
> 5 y	10	0	0.00	0.00	10	6.62	100.00	0.0000	8	1	5.56	12.50	7	5.34	87.50	0.0011
Total	159	8	100.00	5.03	151	100.00	94.97	0.0000	149	18	100.00	12.08	131	100.00	87.92	0.0000

Table 5b
List of Panchakarma therapies with their frequencies and duration during the course of Ayurvedic treatment.

Name of Panchakarma Therapy	Total number of patients	Frequency of Panchakarma therapies									
		1 set	2 sets	3 sets	4 sets	5 sets	6 sets	7 sets	8 sets	9 sets	10 sets
Basti	222	103	47	37	23	3	4	2	1	1	1
Vamana	6	5	0	1	0	0	0	0	0	0	0
Virechana	3	2	1	0	0	0	0	0	0	0	0
Raktamokashana	5	5	0	0	0	0	0	0	0	0	0
Nasya	85	36	24	12	12	1	0	0	0	0	0

Name of Panchakarma Therapy	Duration of Panchakarma therapies (in various sets)									
	1 day	3 days	4 days	5 days	6 days	7 days	10 days	14 days	21 days	28 days
Basti	0	28	0	0	0	165	3	221	1	1
Vamana	6	0	0	0	0	0	0	0	0	0
Virechana	3	0	0	0	0	0	0	0	0	0
Raktamokashana	3	0	2	0	0	0	0	0	0	0
Nasya	1	4	0	2	2	158	0	4	0	0

effects [26]. The known adverse drug reactions together with decreased immune function may be anticipated to occur in these patients and may eventually raise the mortality risk because of profoundly weakened natural immunity in comorbid diseases and concurrent consumption of additional medicines by the patients [27]. Additionally, the binding of the pathogenic SARS-CoV-2 virus with its target cells into the human body is expedited by the ACE-2 receptor. Diabetic or hypertensive patients taking angiotensin II type-I receptor blockers (ARBs) and ACE inhibitors (ACEIs) mostly elevate ACE-2 levels [28,29]. In such patients, increased ACE-2 may worsen SARS-CoV-2 infection. Patients with COVID-19 who had hypertension had higher rates of extensive pneumonia, extreme inflammatory reactions, mutilated organs/tissue, and progressive disease than non-hypertensives [30]. In our study, around 3/4th of cancer patients had comorbidities, especially hypertension and diabetes. Though most of the COVID-19-positive cancer patients in this study were between 40 and 60 years old (around 45 % in both waves) and approximately half of them had one or more than two comorbidities, they showed significant ($p < 0.0001$) resistance to COVID-19 and its complications.

It has been reported that chronic use of alcohol, tobacco, and other drugs is linked to metabolic (diabetes, hypertension), pulmonary (COPD, cardiac insufficiency, and myocardial infarction), and cardiovascular (arrhythmias, cardiac insufficiency, and myocardial infarction) diseases. It can be assumed that people with substance abuse are more likely to experience negative COVID-19 outcomes [31]. In our study, even though the majority of the patients had addictions, very few of them presented with severe COVID-19 manifestations who had taken or were presently on Ayurvedic treatment. This highlights the efficacy of Ayurvedic medicines and therapies in improving and maintaining immunity probably by enhancing the natural killer cells and helper T cells in immunocompromised status [32].

A study in the United States reported that COVID-19 patients who recently received conventional cancer treatment showed a statistically significant rise in the risk of death and ICU admission. On the other hand, patients with no recent cancer treatment had a similar risk of mortality and ICU stay but a lower peril of mechanical ventilation and hospitalization [33]. Conventional cancer therapy is known to hamper the general immunity of patients [34]. In our study, approximately 1/5th of the patients was undergoing conventional cancer treatment during both waves. Of these, the maximum number of patients i.e., 85% and 95% during the 1st and 2nd waves, respectively, were COVID-19 negative. This also proves the efficacy of Ayurvedic medicines as antioxidant and immunomodulatory thereby, improving the quality of life of these patients during their active cancer treatment.

The mortality rates were a mere 0.86% and 0.43% in the respective waves. Considering the availability of vaccinations during the second wave, the rate of mortality might have been reduced. However, accounting for the reported mortality of 14.52% of cancer patients with COVID-19 [35], the mortality rate of less than 1% in our study can be very encouraging.

4.2. Probable mode of action of Ayurvedic treatment to cancer patients in preventing COVID-19 infection

4.2.1. Pathophysiology of SARS-cov-2

Viral infections in the respiratory tract like SARS-CoV-2, modify the immune regulatory network, causing alterations in lymphocyte subpopulations, diminished responsiveness, and lowered macrophage function [36]. Clinically, SARS-CoV-2 infection triggers an immunological response that manifests as two phases viz., the initial phase of immune defence-based protection and the later phase of inflammation-driven destruction [37]. Immunoglobulin IgM and IgG antibodies that attach to SARS-CoV-2 are recruited in the initial phase [38] while in the subsequent phase, uncontrolled cytokines release results in Cytokine Release Syndrome (CRS) or popularly called “cytokine storm” marked by increased IL-2, IL-7, granulocyte colony-stimulating factor, IFN-gamma, and TNF-alpha levels [39]. CRS causes tissue damage in the lungs, kidneys, and heart, resulting in multi-organ failure. COVID-19 causes significant alveolar destruction, which results in Acute Respiratory Distress Syndrome (ARDS) and respiratory failure. One of the ways to restore immunological homeostasis is the restoration of Th1/Th-2 cytokine balance [40,41].

4.2.2. Probable effect of varied Ayurvedic treatment on cancer patients in the present study

The main goal of Ayurvedic medicine in cancer is to boost immunity [42] Therefore, an Ayurvedic method of cancer treatment focuses on improving digestion, removing toxins, limiting tumor growth, and boosting tissue metabolism [43]. All the patients in the current study received Ayurvedic treatment in the form of *Shamana, Rasayana,* and *Panchakarma* as per the individual treatment modality. *Shamana chikitsa* lays the foundation for strengthening immunity by rekindling digestive fire, ensuring good food absorption and assimilation in immunocompromised cancer patients. *Shaman* therapies place a strong emphasis on achieving *Dosha* and *Dhatu* balance within the body at the point of vitiation through the use of oral medications. It is usually implemented successfully when the disease is diagnosed early and *Doshas* are less vitiated. In the advanced stage of the disease, *Shamana chikitsa* in the form of *Deepana* and *Pachana* is mainly administered to improve digestion and metabolism [44]. Thereby probably also helps in combating COVID-19 infestation [45]. A change in diet and lifestyle is also a component of the strategy in addition to medications. *Rasayana* refers to the path of achieving superior *Rasadi Dhatus* (body tissues). Several secondary characteristics of *Rasayana,* such as those that promote lifespan, strength, *Ojabala* (increased vigor), and other benefits, are brought about by the increased nutritional state and the enhanced

Table 6
Co-morbidities in cancer patients analyzed during 1st and 2nd wave of COVID-19 pandemic.

Type of comorbidity	1st wave								2nd wave							
	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi Square Test	No. of patients assessed (n)	COVID-19 positive patients			COVID-19 negative patients			Chi Square
		(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
Diabetes Mellitus	140	4	11.76	2.86	136	20.42	97.14	0.0000	136	20	30.77	14.71	116	20.03	85.29	0.0000
Hypertension	209	2	5.88	0.96	207	31.08	99.04	0.0000	196	21	32.31	10.71	175	30.22	89.29	0.0000
Hypo/ Hyperthyroidism	58	2	5.88	3.45	56	8.41	96.55	0.0000	57	5	7.69	8.77	52	8.98	91.23	0.0000
Asthma	8	1	2.94	12.50	7	1.05	87.50	0.0000	7	1	1.54	14.29	6	1.04	85.71	0.0000
More than two co-morbidities	121	5	14.71	4.13	116	17.42	95.87	0.0000	87	14	21.54	16.09	73	12.61	83.91	0.0000
No Comorbidity	365	15	44.12	4.11	350	52.55	95.89	0.0000	337	32	49.23	9.50	305	52.68	90.50	0.0000

CANCER PATIENTS UNDERGOING CONVENTIONAL THERAPY

Type of comorbidity	1st wave								2nd wave							
	Patients undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi Square Test	Patients undergoing conventional therapy (n)	COVID-19 positive patients			COVID-19 negative patients			Chi-Square
		(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)			(n)	% (Within Positive patients)	% (Within stage)	(n)	% (Within negative patients)	% (Within stage)	
Diabetes Mellitus	37	2	25.00	5.41	35	23.18	94.59	0.0000	36	4	22.22	11.11	32	24.43	88.89	0.0000
Hypertension	46	1	12.50	2.17	45	29.80	97.83	0.0000	40	1	5.56	2.50	39	29.77	97.50	0.0000
Hypo/ Hyperthyroidism	12	0	0.00	0.00	12	7.95	100.00	0.0000	11	0	0.00	0.00	11	8.40	100.00	0.0000
Asthma	1	0	0.00	0.00	1	0.66	100.00	1.0000	0	0	0.00	0.00	0	0.00	0.00	1.0000
More than two co-morbidities	33	1	12.50	3.03	32	21.19	96.97	0.0000	35	7	38.89	20.00	28	21.37	80.00	0.0000
No co-morbidity	85	5	62.50	5.88	80	52.98	94.12	0.0000	80	6	33.33	7.50	74	56.49	92.50	0.0000

Table 7
Vaccination status in cancer patients analyzed during 2nd wave.

Vaccination status	No. of patients assessed (n)	COVID-19 positive patients (n)	% (Within Positive patients)	% (Within vaccination status)	COVID-19 negative patients (n)	% (Within negative patients)	% (Within vaccination status)	Chi-Square test
Yes	526	56	86.15	10.65	470	81.17	89.35	0.0000
No	118	9	13.85	7.63	109	18.83	92.37	0.0000
Total	644	65	100.00	10.09	579	100.00	89.91	0.0000
Cancer patients undergoing conventional therapy								
Vaccination status	No. of patients assessed (n)	COVID-19 positive patients (n)	% (Within Positive patients)	% (Within vaccination status)	COVID-19 negative patients (n)	% (Within negative patients)	% (Within vaccination status)	Chi-Square test
Yes	105	13	72.22	12.38	92	70.23	87.62	0.0000
No	44	5	27.78	11.36	39	29.77	88.64	0.0000
Total	149	18	100.00	12.08	131	100.00	87.92	0.0000

properties of tissues [46]. *Panchakarma* (purificatory therapy) helps to clean and rejuvenate the *Srotasa* (body channels) thus ensuring optimal metabolite transfer [47].

Coronaviruses are a group of RNA viruses [48]. By interacting with the COVID-19 proteases' active site, the majority of *Rasayana* medications block RNA production and replication [49]. SARS-CoV-2 has a significant impact on the T cells, notably $CD4^+$ and $CD8^+$ of the immune system which play an important antiviral action in battling infections. However, it is associated with an increased risk of an inflammatory or autoimmune response [50]. It has also been discovered that $CD4^+$ T helper cells are necessary for the production of SARS-CoV-specific neutralizing antibodies [51]. *Rasayana* herbs promote non-specific immunity. Natural killer (NK) cells are responsible for non-specific innate resistance, but they are also involved in adaptive immunity by supporting the formation of antigen-specific Th1 cells through IFN- and IL-2 production. Improved response of NK effector cells via IFN production and cytotoxic granule exocytosis probably leads to direct neutralization of the virus [52].

The five cleansing techniques of *Panchakarma* based on their specific indications, are applied to various medical conditions like cancer. The elimination of endotoxins from the body is the primary goal of *Panchakarma*. Effective *Panchakarma* lowers oxidative stress, cellular hypoxia, inflammatory cytokine accumulation (preventing cytokine storm), and premature cellular damage [53]. Thus, probably helps in prevention as well as better recovery from COVID-19 infection.

4.3. Limitations of the study

Patients who had discontinued the treatment and were not under regular follow-up or those who received treatment for less than 6 months were excluded from the study as effect of Ayurvedic medicines could not be properly studied in these patients.

4.4. Future scope of research

The Ayurvedic medicines in the form of *Rasayana* and *Shamana Chikitsa* used in the present cohort of cancer patients need to be further studied to understand the mechanisms in reducing COVID-19 infection and actively recommended as the first-line treatment in cancer patients during such kind of pandemics.

5. Conclusion

This study provides insights into the efficacy of Ayurvedic intervention in vulnerable or high-risk cancer patients against COVID-19 in terms of low incidence, less severity, less aggressive intervention required, and low mortality.

Source of funding

None.

Author contribution

Author 1–SS, Author 2-VD and Author 3- VG: Conception or design of the work, Drafting the work or revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work,

Author 4-VG, Author 5-SG, Author 6- SK, Author 13- SD: Conception or design of the work, Acquisition of the work, analysis, interpretation, drafting the work or revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work.

Author 8 – NS, Author 9- BS: Acquisition of the work, analysis, interpretation of data for the work, drafting the work or revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work,

Author 7 –SD, Author 10 –SB, Author 11– SC, Author 12 – VA, Author 14 – AS, Author 15-AS, Author 16- AS, Author 17- SN, Author 18- DD, Author 19-TD: Analysis, drafting the work or revising it critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author did not use generative AI in the paper.

Declaration of competing interest

The authors have no conflict of interest.

Acknowledgement

The authors acknowledge the help of statistician Mr. Sagar Khandagale, M. Sc. – Statistics (Director, Markov Research and Analytics Services (OPC) Pvt Ltd. Pune- 411 028) and our team in the treatment and follow-up of the patients. Special thanks to Dr. Sameer Gore, Dr. Sanjog Awalkanthe, Dr. Vijay Radye, Dr Suchita Shiraskar, Miss Swati Chaudhari, Mrs. Sunita Chavan, Mr. Abhijeet Ghodke and Mr. Sumeet Ghodke. We also thank Mr. Shyam Shitole for helping out in preparing the figures.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

org/10.1016/j.jaim.2024.101045.

References

[1] Al-Quteimat OM, Amer AM. The impact of the COVID-19 pandemic on cancer patients. Am J Clin Oncol 2020;43:452–5. https://doi.org/10.1097/COC.0000000000000712.

[2] Jha P, Deshmukh Y, Tumbe C, Suraweera W, Bhowmick A, Sharma S, et al. COVID mortality in India: national survey data and health facility deaths. Science 2022;375:667–71. https://doi.org/10.1126/science.abm5154.

[3] Monto J. Major causes of influenza and its various classifications. J Health Commun 2023;8:80015. https://doi.org/10.36846/2472-1654-8.2.8015.

[4] Epidemiology Working Group for NCIP Epidemic Response Epidemiology Team. The Epidemiological Characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China, 2020. China CDC Wkly 2020;2:113–22. PMID: 34594836.

[5] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21:335–7. https://doi.org/10.1016/S1470-2045(20)30096-6.

[6] Russell B, Moss CL, Shah V, Ko TK, Palmer K, Sylva R, et al. Risk of COVID-19 death in cancer patients: an analysis from guy's cancer centre and king's college hospital in london. Br J Cancer 2021;125:939–47. https://doi.org/10.1038/s41416-021-01500-z.

[7] Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. Cancer Discov 2020;10:783–91. https://doi.org/10.1158/2159-8290.CD-20-0422.

[8] Chan KW, Wong VT, Tang SCW. COVID-19: an update on the epidemiological, clinical, preventive and therapeutic evidence and guidelines of integrative Chinese–Western medicine for the management of 2019 novel coronavirus disease. Am J Chin Med 2020;48:737–62. https://doi.org/10.1142/S0192415X20500378.

[9] Dornala SN, Ayyagari R. Guidelines for safer panchakarma practice in non-covid clinical care during corona pandemic. J Ayurveda Integr Med 2022;13:100426. https://doi.org/10.1016/j.jaim.2021.03.008.

[10] Thakar A, Panara K, Patel F, Bhagiya S, Goyal M, Bhinde S, et al. Add-on Ayurveda treatment for early stage COVID-19: a Single center retrospective cohort study from Gujarat, India. J Evid Based Integr Med 2021;26:1–7. https://doi.org/10.1177/2515690X211020685.

[11] Guilmoto CZ. An alternative estimation of the death toll of the Covid-19 pandemic in India. PLoS One 2022;17:1–14. https://doi.org/10.1371/journal.pone.0263187.

[12] Skrivankova VW, Richmond RC, Woolf BAR, Davies NM, Swanson SA, VanderWeele TJ, et al. Strengthening the reporting of observational studies in epidemiology using mendelian randomisation (STROBE-MR): explanation and elaboration. BMJ 2021:n2233. https://doi.org/10.1136/bmj.n2233.

[13] De Sanctis V, Soliman AT, Daar S, Tzoulis P, Fiscina B, Kattamis C, et al. Retrospective observational studies: lights and shadows for medical writers. Acta Biomed 2022;93:e2022319. https://doi.org/10.23750/abm.v93i5.13179.

[14] Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009;41:1149–60. https://doi.org/10.3758/BRM.41.4.1149.

[15] Ullgren H, Camuto A, Rosas S, Pahnke S, Ginman B, Enblad G, et al. Clinical characteristics and factors associated with COVID-19-related death and morbidity among hospitalized patients with cancer: a Swedish cohort study. Acta Oncol (Madr) 2021;60:1459–65. https://doi.org/10.1080/0284186X.2021.1958005.

[16] Ehmsen S, Jakobsen LH, Lendorf ME, Eefsen RL, Bentsen L, Knoop AS, et al. Severity and 1-month outcome of SARS-CoV-2 infection in patients with solid cancers: a Danish nationwide cohort study. Acta Oncol (Madr) 2021;60:859–65. https://doi.org/10.1080/0284186X.2021.1889659.

[17] Ferrari BL, Ferreira G, Menezes M, De Marchi P, Canedo J, et al. Determinants of COVID-19 mortality in patients with cancer from a community Oncology practice in Brazil. JCO Global Oncol 2021;7:46–55. https://doi.org/10.1200/GO.20.

[18] Zhang H, Han H, He T, Labbe KE, Hernandez AV, Chen H, et al. A Systematic Review and Meta-Analysis. J Natl Cancer Inst 2021;113:371–80. https://doi.org/10.1093/jnci/djaa168.

[19] Lee LYW, Cazier JB, Angelis V, Arnold R, Bisht V, Campton NA, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet 2020;395:1919–26. https://doi.org/10.1016/S0140-6736(20)31173-9.

[20] Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020;395:1907–18. https://doi.org/10.1016/S0140-6736(20)31187-9.

[21] Robilotti EV, Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M, et al. Determinants of COVID-19 disease severity in patients with cancer. Nat Med 2020;26:1218–23. https://doi.org/10.1038/s41591-020-0979-0.

[22] Martin S, Kaeuffer C, Leyendecker P, Tuzin N, Tazi Y, Schaff-Wendling F, et al. COVID-19 in patients with cancer: a retrospective study of 212 cases from a French SARS-CoV-2 cluster during the first wave of the COVID-19 pandemic. Oncol 2021;26:1656–9. https://doi.org/10.1002/onco.13831.

[23] Lee KA, Ma W, Sikavi DR, Drew DA, Nguyen LH, Bowyer RCE, et al. Cancer and risk of COVID-19 through a general community survey. Oncol 2021;26:182–5. https://doi.org/10.1634/theoncologist.2020-0572.

[24] Tian J, Yuan X, Xiao J, Zhong Q, Yang C, Liu B, et al. Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study. Lancet Oncol 2020;21:893–903. https://doi.org/10.1016/S1470-2045(20)30309-0.

[25] Martín-Moro F, Marquet J, Piris M, Michael BM, Sáez AJ, Corona M, et al. Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies. Br J Haematol 2020;190:16–20. https://doi.org/10.1111/bjh.16801.

[26] Chavda VP, Kapadia C, Soni S, Prajapati R, Chauhan SC, Yallapu MM, et al. A global picture: therapeutic perspectives for COVID-19. Immunotherapy 2022;14:351–71. https://doi.org/10.2217/imt-2021-0168.

[27] Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis. Intervirology 2021;64:36–47. https://doi.org/10.1159/000512592.

[28] Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8:21. https://doi.org/10.1016/S2213-2600(20)30116-8.

[29] Li XC, Zhang J, Zhuo JL. The Vaso protective axes of the renin-angiotensin system: physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases. Pharmacol Res 2017;125:21–38. https://doi.org/10.1016/j.phrs.2017.06.005.

[30] Huang S, Wang J, Liu F, Liu J, Cao G, Yang C, et al. COVID-19 patients with hypertension have more severe disease: a multicentre retrospective observational study. Hypertens Res 2020;43:824–31. https://doi.org/10.1038/s41440-020-0485-2.

[31] Wang QQ, Kaelber DC, Xu R, Volkow ND. COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States. Mol Psychiatr 2021;26:30–9. https://doi.org/10.1038/s41380-020-00880-7.

[32] Vallish BN, Dang D, Dang A. Nature and mechanism of immune boosting by Ayurvedic medicine: a systematic review of randomized controlled trials. World J Methodol 2022;12:132–47. https://doi.org/10.5662/wjm.v12.i3.132.

[33] Chavez-MacGregor M, Lei X, Zhao H, Scheet P, Giordano SH. Evaluation of COVID-19 mortality and adverse outcomes in US patients with or without cancer. JAMA Oncol 2022;8:69. https://doi.org/10.1001/jamaoncol.2021.5148.

[34] Harris J, Sengar D, Stewart T, Hyslop D. The effect of immunosuppressive chemotherapy on immune function in patients with malignant disease. Cancer 1976;37(Suppl 2):1058–69. https://doi.org/10.1002/1097-0142(197602)37:2+<1058::aid-cncr2820370813>3.0.co;2-o.

[35] Mehta A, Vasudevan S, Parkash A, Sharma A, Vashist T, Krishna V. COVID-19 mortality in cancer patients: a report from a tertiary cancer centre in India. PeerJ 2021;9:10599. https://doi.org/10.7717/peerj.10599.

[36] Zhou Y, Fu B, Zheng X, Wang D, Zhao C, Qi Y, et al. Pathogenic T-cells and inflammatory monocytes incite inflammatory storms in severe COVID-19 patients. Natl Sci Rev 2020;7:998–1002. https://doi.org/10.1093/nsr/nwaa041.

[37] Shi Y, Wang Y, Shao C, Huang J, Gan J, Huang X, et al. COVID-19 infection: the perspectives on immune responses. Cell Death Differ 2020;27:1451–4. https://doi.org/10.1038/s41418-020-0530-3.

[38] Long QX, Tang XJ, Shi QL, Li Q, Deng HJ, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med 2020;26:1200–4. https://doi.org/10.1038/s41591-020-0965-6.

[39] Ritchie AI, Singanayagam A. Immunosuppression for hyperinflammation in COVID-19: a double-edged sword? Lancet 2020;395:1111. https://doi.org/10.1016/S0140-6736(20)30691-7.

[40] Kidd P. Th1/Th2 balance: the hypothesis, its limitations, and implications for health and disease. Alternative Med Rev 2003;8:223–46.

[41] Spellberg B, Edwards JE. Type 1/Type 2 immunity in infectious diseases. Clin Infect Dis 2001;32:76–102. https://doi.org/10.1086/317537.

[42] Vallish BN, Dang D, Dang A. Nature and mechanism of immune boosting by Ayurvedic medicine: a systematic review of randomized controlled trials. World J Methodol 2022;12:132–47. https://doi.org/10.5662/wjm.v12.i3.132.

[43] Dhruva A, Hecht FM, Miaskowski C, Kaptchuk TJ, Bodeker G, Abrams D, et al. Correlating traditional Ayurvedic and modern medical perspectives on cancer: results of a qualitative study. J Alternative Compl Med 2014;20:364–70. https://doi.org/10.1089/acm.2013.0259.

[44] Upadhayay Y. editor Ashtang Hrudayam of Vagabhata. Sutra Sthana, Dwividhaupakramaniya Adhyaya. eleventh ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1993. p. 101 [Chapter 14], Verse 6.

[45] Sharma M, Sharma C, Mandal SK, Nesari TM, Kumar A. Immune status determined as per guidelines of Ayurveda found associated with clinical outcomes of COVID-19 disease – results of a cross-sectional pilot study. J Ayurveda Integr Med 2022;13:100425. https://doi.org/10.1016/j.jaim.2021.03.007.

[46] Tripathi B, editor. Charaka Samhita of Agnivesha, chikitsa Sthana; Rasayan Adhyaya. fourth ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1996. 5, [Chapter 1], Verse 7-8.

[47] Tripathi B. Charaka Samhita of Agnivesha. fourth ed. Varanasi: Chaukhambha Sanskrit Sansthan; 1996. p. 185. Sutra Sthana; Navegandharniya Adhyaya: [Chapter 7], Verse 49.

[48] Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol 2020;92:424–32. https://doi.org/10.1002/jmv.25685.

[49] Panda AK, Kar S. Ayurvedic immuno booster: is it myth or reality in COVID-19 pandemic. Int J Curr Res Rev 2021;13:134–40. https://doi.org/10.31782/IJCRR.2021.13140.

[50] Cecere TE, Todd SM, LeRoith T. Regulatory T cells in arterivirus and coronavirus infections: do they protect against disease or enhance it? Viruses 2012;4:833–46. https://doi.org/10.3390/v4050833.

[51] Janice Oh HL, Ken-En Gan S, Bertoletti A, Tan YJ. Understanding the T cell immune response in SARS coronavirus infection. Emerg Microb Infect 2012;1:1–6. https://doi.org/10.1038/emi.2012.26.

[52] Singh R, Goel S, Bourgeade P, Aleya L, Tewari D. Ayurveda Rasayana as antivirals and immunomodulators: potential applications in COVID-19. Environ Sci Pollut Control Ser 2021;28:55925–51. https://doi.org/10.1007/s11356-021-16280-5.

[53] T Nesari, Kajaria D. Combating COVID-19 with holistic approach of Ayurveda. Indian Journal of Traditional Knowledge 2021;19. https://doi.org/10.56042/ijtk.v19i0.36019.