Online Yoga and Ayurveda Intervention as Tertiary Prevention of Psychological Comorbidities in COVID-19 Survivors: A Randomized Controlled Trial

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Abstract

Background and Purpose: About 56% of symptomatic COVID-19 survivors have been found with neuropsychological comorbidities, such as depression, anxiety, posttraumatic stress disorders (PTSD), and impaired quality of life (QoL). Alongside, antimicrobial, anti-inflammatory, neuroprotective, regenerative, immunomodulatory, cardio-pulmonary health promotive, and psychological benefits of yogic and Ayurvedic intervention are well documented. Therefore, this study aimed to assess the effect of online Yoga (OYI) and Yoga cum Ayurveda intervention (OYAI) on COVID-19-induced depression, anxiety, PTSD, and poor QoL.

Method: Seventy-two participants (males/females: 33/26) with at least a 3-month back history of symptomatic COVID-19 infection and age (mean ± SD: 32.33 ± 9.9 and 33.04 ± 12.9 for males and females, respectively) were recruited from Patanjali Ayurveda Hospital, Haridwar, India, and All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India, before random allocation into an equal-sized control group (CG), Yoga group (YG) and Yoga cum concoction (YCG) group. Split-plot analysis of variance and Kruskal–Wallis tests with Bonferroni adjusted *post hoc* comparisons were computed for normal and nonnormal data using IBM SPSS (25th Version, SPSS South Asia Private Limited, Bangalore, India).

Results: Both the treatments—the 30-day OYI and OYAI, significantly improved depression ($P < .002$, ES: -0.99 and $P < .001$, ES: -2.11), anxiety ($P < .001$, ES: -1.32 and -1.89), PTSD ($P < .001$, ES: -1.8 and -1.83) and QoL related constructs ($P < .001$, ES: 0.63 and 0.76; 0.71 and 0.93 for each OYI and OYAI versus general health and physical health; $P < .001$, ES: 0.65 for OYAI versus psychological health; and $P < .003$, ES: 0.54 for OYI versus environment) of the participants compared to the controls.

Conclusion: OYAI may better ameliorate COVID-19-induced psychological comorbidities than OYI with no adverse effects.

Keywords

COVID-19 survivors, Psycho-neuropathology, Yoga, Psychosomatic, Ayurveda

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Introduction

About 56% of COVID-19 survivors have been diagnosed with one clinically crucial psychopathological comorbidity such as anxiety (42%), insomnia (40%), depression (31%), posttraumatic disorder (PTSD) (28%), and OCD (20%).[1] Another study consistently reported that 22.7%, 21.7%, 20.8%, and 16.2% of people exposed to restrictive measures for managing pandemic infections had clinically significant depression, PTSD, psychological distress, and anxiety, respectively.[2] Fear of COVID-19 infection, social distancing, familial isolation, prohibition of everyday sports activities, financial loss, uncertain job, and future, disrupted regular routines, and brain changes caused by the COVID-19 infection are commonly reported triggers for the onset of

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psychological comorbidities[3,4] and poor quality of life (QoL). The neuropsychiatric pathology, immunological host responses, and some treatment modalities developed because of the COVID-19 outbreak declined COVID-19 survivors' QoL.[5,6] Attack of SARS-Cov-2 on angiotensin-converting enzyme receptors-II (ACE-II), alveolar epithelia, and vascular endothelial eventually induce severe acute respiratory distress, stroma, and sepsis, thereby leading to restricted oxygen supply to brain, liver, heart, kidney, and other vital organs.[7] COVID-19 infection may spread to the brain via the olfactory bulb/nerve and cause neuronal damage or death.[8] SARS-CoV-2 in the olfactory bulb polarizes microglial cells toward an inflammatory phenotype, impairing brain morphology and causing neurodegenerative diseases.[9] Cytokines' dysregulation, especially interleukin (IL)—IL-1β, IL-6, and IL-10, interferon-γ (IFN-γ), tumor necrosis factor-*α* (TNF-*α*), and transforming growth factor-β (TGF-β), is associated with psychiatric disorders.[1] Neuroinflammation disrupted blood–brain barrier, invaded peripheral immune cells into the central nervous system, impaired neurotransmission, disturbed hypothalamus-pituitary-adrenal (HPA) axis, microglia stimulation, and induction of indoleamine 2,3-dioxygenase indicate interaction pathways between immune systems and psychopathological mechanism underpinning psychiatric disorders.[1,10]

Commonly reported biomarkers associated with post-COVID-19 depression[11] are increased levels of IL-6, soluble interleukin six receptors (SIL-6R), IL-1β, TNF-*α*, IFN-γ, IL-10, IL-2, soluble interleukin-2 receptors (SIL-2R), C-reactive protein (CRP), monocyte chemoattractant protein-1 (MCP-1), serum amyloid A1 (SAA1), and metabolites of the kynurenine pathway, and decreased brain-derived neurotrophic factor (BDNF) and tryptophan.[11] Elevated D-dimer, IL-6, CRP, and lymphocyte count are the common biomarkers associated with post-COVID-19 anxiety disorders.[1] COVID-19 survivors develop PTSD with common biomarkers—increased corticotropin-releasing factor (CRF) and adrenocorticotropic hormone (ACTH), IL-6, TNF-α, dysfunctional HPA axis, glucocorticoid receptor (GCR/GR) sensitivity, and allele of apolipoprotein E gene (ApoE4), and decreased gamma-aminobutyric acid (GABA), dopamine transporter gene (DAT), trimethylated histone H3 lysine 4 amino acid (H3K27), glial fibrillary acidic protein, natural killer cells (NK cells), and T-helper cells (Th cells) along with serotonergic dysfunction.[11–13] QoL is a multidimensional construct related to the person's physical health, psychological state, level of independence, social relationships, personal beliefs, and relationship to the environment's salient features by including their positive and negative dimensions.[14] The decreased frequency and intensity of exercise and mind-body practices during the COVID-19 pandemic negatively impacted people's physical, mental, spiritual, and social health and overall QoL.

The ancient Indian traditional healing systems—Yoga and Ayurveda, have been projected as immune-modulating and harmless prophylactic treatment options for COVID-19.[15,16] Yoga is a complete set of principles, processes, and practices—such as body cleansing techniques, poses, conscious breath regulations, locks, gestures, sensory withdrawals, concentration/mindfulness, and meditation, that address somatic, psychic, social, and spiritual dimensions of health instrumental for spiritual elevation.[17] Prior studies have reported that integral Yoga intervention might mitigate neuropsychiatric problems, such as depression, stress, anger, and PTSD, of health care workers.[18,19] Yogic loosening and stretching poses synchronized with deep breathing and mental awareness induced antimicrobial effects in respiratory epithelial cells during SARS-Cov-2 infection.[20] The yogic postures, breath regulations, and Omkar meditation significantly increased melatonin and improved cardiorespiratory performance and psychological profile of normotensive practitioners compared to the exercise group.[21] Twelve-week Yoga and meditation-based lifestyle significantly improved neuroplasticity, mind–body communications, and cellular health of the participants with major depressive disorder (MDD).[22] Twelve-week Iyengar Yoga intervention significantly increased the thalamic GABA level and decreased depression scores of the practitioners with MDD.[23,24] A set of three breath regulatory practices—Sudarshan Kriya, is claimed to modulate vagal tone, elevate GABA levels,[25] decrease stress hormones,[26] and empower immune functions by upregulating antioxidant markers, gene expression, and telomerase reverse transcriptase (hTERT).[27] Besides, Ayurveda aims to maintain optimal health, enhance longevity, and heal diseases by using detoxification procedures, mineral/herbal formulations, and lifestyle cum dietary moderation. The recently published meta-analysis, including 32 RCTs with 3177 COVID-19 patients, projected herbal medicines as a harmless add-on therapy for better ameliorating inflammatory markers and clinical symptoms of COVID-19 compared to independent standard care (SC).[28] The specific phytochemicals and herbal formulations prescribed in Ayurvedic texts effectively mitigate neuropsychiatric illnesses.[29,30] Ashwagandha (*Withania sominfera*), Guduchi (*Tinospora cordifolia*), Tulsi (*Ocimum tenuiflorum*), seabuckthorn (*Hippophaes rhamnoides*), raisins (*Vitis vinifera*), Mulethi (*Licorice*), black pepper (*Piper nigrum L*), and ginger (*Zingiber officinal*) are the prominent medicinal plants containing vital phytochemicals with antimicrobial, antiviral, disinfectant, anti-inflammatory, neuroprotective, antidepressive, anxiolytic, atherosclerotic, hepatoprotective, antioxidant, immunomodulatory, analgesic, regenerative, appetizing, rejuvenating, and pharmacotherapeutic effects on COVID-19 infections and its neuropsychiatric comorbidities.[16,31–39] Reducing SARS-Cov-2 infection, inflammation, cytokine storm, degeneration, and distress using these Ayurvedic formulations might mitigate COVID-19-induced neuropsychiatric comorbidities.

These findings suggest that integral Yoga and Yoga cum Ayurveda intervention might ameliorate symptomatic COVID-19 infection and post-COVID-19 neuropsychiatric

problems. Essentially, randomized controlled trials (RCTs) that report the independent or combined effect of online integral Yoga and Ayurveda intervention on COVID-19-induced neuropsychiatric problems are scarce. Therefore, this three-armed (Yoga Group: YG, Yoga and Concoction Group: YCG and Control Group: CG) RCT aimed to assess the effects of online Yoga intervention (OYI) and online Yoga Ayurveda intervention (OYAI) as tertiary prevention of COVID-19—induced depression, anxiety, PTSD, and poor QoL. In this context, tertiary prevention refers to care that reduces disability and morbidity in people diagnosed with and treated for COVID-19-induced neuropsychiatric diseases.[40]

Methods

Participants, Setting, and Design

Out of 206 patients recruited from outpatient departments (OPDs) of Patanjali Ayurveda Hospital, Haridwar, India, and Psychiatry Department of All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India (from November 2021 to January 2022), 72 participants with BDI scores ≥10 and demographic details depicted in Table 1 were randomly allocated into equal-sized YG, YCG, and CG by using Random Allocation Software (RAS; Figure 1: CONSORT Flowchart).[41] For random allocation, entries with sample size: 72, groups: 3, random size: 24, format: 1 column and 1 cell spacing, and code: sequential numeric were set and run in RAS in September 2021.

Table 1. Demographic Details of the Participants.

Demographic Data	YG *n* (Mean ± SD)	YCG *n* (Mean ± SD)	CG *n* (Mean ± SD)
Gender (56% males)			
Male (age in years)	09 (29.7 ± 6.2)	10 (31.7 ± 11.3)	14 (34.4 ± 11)
Female (age in years)	10 (34.1 ± 15.1)	11 (34 ± 11.8)	05 (28.6 ± 12)
Baseline BDI Score	19 (23.74 ± 9.01)	21 (20.05 ± 5.53)	19 (21.47 ± 8.8)
Education			
Higher secondary	01	03	01
Undergraduate	11	08	06
Postgraduate	04	08	05
PhD	00	00	01
Other	03	02	06
Residence			
Urban	15	11	15
Rural	04	10	04

Abbreviations: YG, Yoga group; YCG, Yoga and concoction group; CG, control group; M ± SD, mean ± standard deviation.

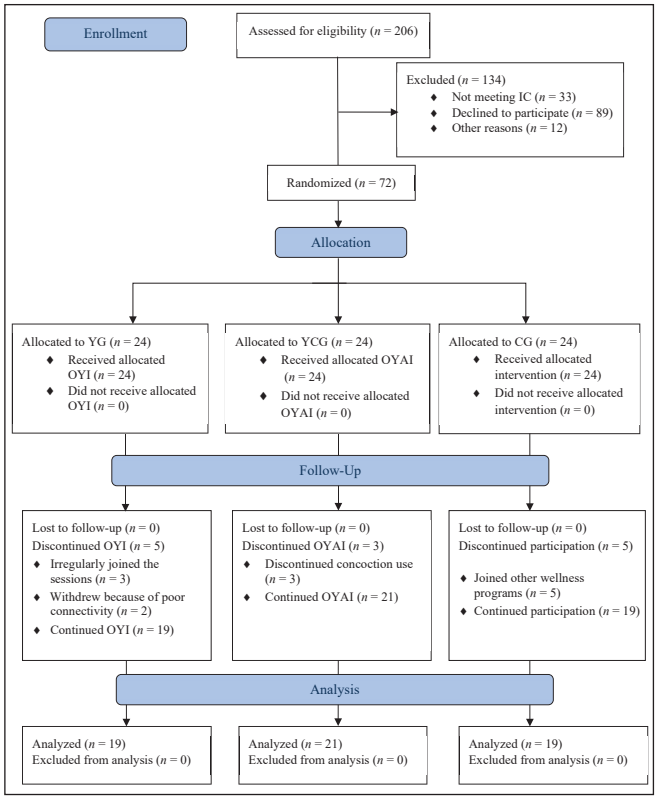

Figure 1. CONSORT Diagram.

Patients went through the participant's information sheet and voluntarily signed the informed consent form before collecting data. The mean ± SD regarding baseline BDI scores of YG, YCG, and CG were 23.74 ± 9.01, 20.05 ± 5.53, and 21.47 ± 8.8, respectively. Of 72 participants, 13 (5 in YG, 5 in CG, and 3 in YCG) dropped out and 59 (33 males and 26 females aged 32.33 ± 9.9 and 33.04 ± 12.9 years) participated till the study completion. The study was approved by the Institutional Ethics Committee of the University of Patanjali (Ref. No.: UOP/IEC/2021/01) and registered in Clinical Trials Registry-India (CTRI/2021/05/033793).

Inclusion Criteria (IC)

Interested symptomatic COVID-19 survivors with age range 18 to 65 years, BDI score ≥10,[42] no prior habit of exercise, Yoga, and Ayurvedic medicines, an email address, Wi-Fi-enabled smartphone/computer, and Zoom interface operating skills were scanned and included.

Exclusion Criteria (EC)

Participants with age ≤18 or ≥ 65, disability, pregnancy/lactating phase, prior habits of Yoga and physical activity, and history of medical illnesses, such as neurological, psychiatric, hypertension, diabetes mellitus, cardiovascular disease, renal complications, liver disorders, locomotors disabilities,

glaucoma, hernia, gut ulcers, recent surgery, and addictive behaviors, before the onset of COVID-19 clinical symptoms were excluded.

Intervention Protocol

Duration: February 2, 2022 to March 6, 2022, Timing: 7:00 to 8:30 AM, five days a week.

Commencing prayer (05 min).: Omkar, Gayatri Mantra and Guru Vandana.

Somatic Practices (30 min)

Loosening and energizing series (LES), i.e., 30 whole-body stretches for joint mobilization and energy generation, alligator twists,[43–46] and sun salutation (SN); other poses: cat, tiger, monkey, mountain, palm tree, head to toe, camel, chair, rabbit, half palm tree, cobra, locust, seated semi spinal twist, thunderbolt, and crocodile.[47] The practice of the poses was synchronized with customized deep breathing and mental awareness (30 min).

Energy Practices (15 min)

Pranayams: uninostril (UNB), alternate nostril (ANB),[48] Kapalbhati (high-frequency Yoga breathing: HFYB), Bhastrika (forceful deep breathing: FDB), Dhriti Shakti Vikasak (crown breathing: CB), Ujjayi (coherent breathing), Bhramari (resonance breathing: RB); Mudras: Shaktichalini (external anal sphincter lock: EASL), Jnyan, and Sanmukhi; and Bandhas: perineal lock (PL), throat lock (TL), and abdominal lock (AL).[47]

Mental Practices (15 min)

Solar meditation (SM).[49]

Emotive Practices (25 min)

Instrumental music meditation (IMM), questions and answers, and prayer for peace.[49]

The Yoga protocol was administered online in parts commencing from LES, alligator twists, three breath regulations (UNB, ANB, and coherent), EASL, PL, and IMM a day, and SN, rest postures, four breath regulations (FDB, HFYB, CB, and RB), EASL, PL, TL, AL, and SM on every alternate day. Weekends were left for participants' self-practice.

Composition of the Herbal Formulation

A mixture of 2500 g Ashwagandha powder, 2600 g Guduchi Kwath, 1000 g Tulsi ghanvati powder, 2500 g Mulethi Kwath, 600 g Shunthi powder, 600 g black pepper powder, and 3250 g raisins manufactured/marketed by Patanjali Ayurved Limited, Haridwar, India, and 5000 g dried sea buckthorn fruit procured from local market of Leh Ladakh, India, was prepared for 25 persons.

Herbal mixture of 700 g was mailed to each YCG participant to drink 200 mL concoction daily for 30 days. The participants were advised to put five teaspoons (24 g) daily in 1 L of water for slow boiling till it reached 200 mL. A dose of 100 mL before 30 min to 60 min of each morning and evening meal was prescribed.

Measures and Data Collection

Beck Depression Inventory (BDI), containing 21 items to be responded to on a 4-point Likert scale (0, 1, 2, and 3), was used to measure the depressive symptoms of the participants. The items correspond to the clinical depression symptoms noted in patients, such as loss of interest, difficulty in focusing, and suicidal thoughts. The BDI score ranges of 0 to 9, 10 to 18, 19 to 29, and 30 to 63 imply minimal, mild to moderate, moderate to severe, and severe depression, respectively.[50] The entire items were clustered into two factors: cognitive-affective (16 items) and somatic (5 items).[51] The scale has high construct validity ($\alpha = 0.92$) and test-retest reliability ($r = 0.93$).[52] For the current sample, Cronbach's α were found to be 0.825, 0.470, and 0.833 for the cognitive-affective factor, somatic factor, and overall BDI, respectively.

The Hamilton Anxiety Rating Scale (HAM-A), with 14 items clustered into psychic, somatic, and behavioral symptoms and responded to the five-point Likert scale (0, 1, 2, 3, and 4), was used to measure anxiety. The total HAM-A score range was 0 to 56, wherein each item score could range from 0 (not present) to 4 (very severe).[53] The score ranges of 8 to 14, 15 to 23, and ≥24 suggest mild, moderate, and severe anxiety, respectively.[54] HAM-A had Cronbach's $\alpha = 0.86$.[55] Cronbach's α computed from the current sample were 0.722, 0.859, and 0.859 for psychic anxiety, somatic anxiety, and overall anxiety, respectively.

The WHO-QoL-BREF is a shortened version of WHO-QoL-100. BREF consists of 26 items to be rated from 1 to 5. The 24 items of the scale are factorized into 4 domains: physical health, psychological health, social relationships, and environment. The aggregate score in each of the domains reflects an individual's QoL in that domain. A higher score implies a higher QoL. Each domain's transformed score was calculated by multiplying its average score with four to make all domains comparable. Items I and II were scored separately from 1 to 5, suggesting an individual's general perception of overall QoL and health. The scale was found to be cross-culturally valid with high test–retest reliability for domains ranging from 0.66 (physical health) to 0.87 (environment).[56,57] Cronbach's α computed from the current sample were 0.364, 0.503, 0.581, 0.687, and 0.785 for physical health, psychological health, social relationships, environment, and total QoL, respectively.

The Davidson Trauma Scale (DTS) is a 17-item (clustered into 4 factors—intrusion, avoidance, numbing, and hyperarousal) self-report questionnaire that measures the 17 symptoms of PTSD set by *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. This four-factor model has high internal consistency and reliability.[58] The scale has good test–retest reliability ($r = 0.86$).[59] Each item is measured for its occurrence, i.e., frequency and severity, on a five-point Likert scale. The frequency is measured from 0 ("not at all present") to 4 ("every day") and severity from 0 ("not at all distressing") to 4 ("extremely distressing"). Scores in frequency and severity can be assessed independently with a score range of 0 to 68. The score of a particular item is the summation of its frequency and severity score. The total score of DTS ranges from 0 to 136. Using the current sample, Cronbach's α were found to be 0.598, 0.326, 0.552, 0.584, and 0.802 for intrusion, avoidance, numbing, hyperarousal, and overall DTS, respectively.

The baseline data of 206 patients regarding their case record performa, signed consent form, and BDI were collected during participants' recruitment. After proportionate random allocation of 72 participants meeting IC into CG, YG, and YCG, four online Google forms regarding BDI, HAM-A, WHO-QoL BREF, and DTS were shared via WhatsApp Group before 1 week (the last week of January 2022) of intervention commencement and asked to fill them up during subsequent zoom meetings organized for providing instructions and clarifications. Each participant was provided contact details of the research team to sort out further clarifications and queries. Similarly, the post data were generated within 1 week (the second week of March 2022) after completing a 1-month OYI and OYAI.

Statistical Analysis

A sample size of 72 was computed from G* Power Software (repeated measures between factors) by considering effect size ($\eta^2 = 0.38$),[60] $\alpha = 0.05$, and $\beta = 0.2$ and 30% dropouts. IBM SPSS (25th version, SPSS South Asia Private Limited, Bangalore, India) was used for the entire data analysis regarding hypotheses testing. For the normal data (regarding depression, anxiety, and PTSD and their associated factors) with insignificant Shapiro–Wilk test, Split Plot analysis of variance was used to compute between group (group: CG-1, YG-2, and YCG-3), within-group (time: before-1 and after-2) and interactive effects along with Bonferroni adjusted *post hoc* analyses for inter and intra group pairwise comparisons. Kruskal–Wallis and Bonferroni adjusted Mann–Whitney and Wilcoxon signed-rank tests were computed for nonnormal data regarding QoL and its factors for intergroup and intragroup comparisons.

Results

Table 2. ANOVA Results Regarding Depression, Anxiety, and PTSD.

Outcome Variables	Source of Variation	Sum of Squares	Mean Square	*df*	*F*	η^2
Affective-cognitive depression	G	675.53	337.77	2	4.82ξ	0.147
	T	267.13	267.13	1	48.36□	0.463
	G × T	517.48	258.74	2	46.84□	0.626
	E	3923.52	70.06	56	–	–
Somatic depression	G	64.49	32.25	2	6.17*	0.18
	T	92.68	92.68	1	64.37□	0.535
	G × T	517.48	258.74	2	46.84□	0.291
	E	292.85	5.23	56	–	–
Depression	G	1172.12	586.06	2	5.99*	0.176
	T	468.01	468.01	1	81.48□	0.593
	G × T	811.16	405.58	2	70.61□	0.716
	E	5474.22	97.75	56	–	–
Psychic anxiety	G	138.21	69.11	2	3.71 ξ	0.117
	T	236.64	236.64	1	139.36□	0.713
	G × T	208.19	104.09	2	61.3□	0.686
	E	1043.48	18.63	56	–	–
Somatic anxiety	G	184.42	92.21	2	2.69	0.088
	T	65.09	65.09	1	32.59□	0.368
	G × T	190.43	95.21	2	47.67□	0.630
	E	1915.48	34.21	56	–	–

(Table 2 continued)

(Table 2 continued)

Outcome Variables	Source of Variation	Sum of Squares	Mean Square	*df*	*F*	η^2
Behavioral anxiety	G	5.19	2.59	2	1.91	0.064
	T	1.14	1.14	1	9.15*	0.14
	G × T	4.78	2.38	2	19.1□	0.406
	E	76.25	1.36	56	–	–
Anxiety	G	761.03	380.51	2	4.27ξ	0.132
	T	601.26	601.26	1	111.98□	0.667
	G × T	917.77	458.88	2	85.47□	0.753
	E	4994.09	89.18	56	–	–
Intrusion PTSD	G	126.44	63.22	2	2.28	0.076
	T	196.4	196.4	1	94□	0.627
	G × T	180.76	90.38	2	43.26□	0.607
	E	1547.42	27.63	56	–	–
Avoidance PTSD	G	19.46	9.73	2	1.59	0.054
	T	43.01	43.01	1	60.53□	0.519
	G × T	22.55	11.27	2	15.86□	0.362
	E	342.3	6.11	56	–	–
Numbing PTSD	G	238.57	119.29	2	4.51ξ	0.139
	T	194.25	194.25	1	111.19□	0.665
	G × T	149.07	74.54	2	42.67□	0.604
	E	1481.78	26.46	56	–	–
Hyperarousal PTSD	G	720.64	360.32	2	13.94□	0.332
	T	115.19	115.19	1	42.54□	0.432
	G × T	286.23	143.12	2	52.85□	0.654
	E	1447.05	25.84	56	–	–
PTSD	G	3272.35	1636.17	2	8.11□	0.225
	T	2072.85	2072.85	1	189.18□	0.772
	G × T	2245.3	1122.65	2	102.46□	0.785
	E	11294.41	201.69	56	–	–

Note: *N* = 59, between-group variance = group (G); within group variance = timepoints (T); error variance = error (E), **P* < .01; □*P* < .001; ξ*P* < .05.

Abbreviation: ANOVA, analysis of variance; PTSD, posttraumatic stress disorder.

Table 3. Inter and Intragroup Comparisons Regarding Depression, Anxiety, and PTSD.

	Within Group Effects						Between Group Effects *P*-Value (Effect Size)		
	YG (19)		YCG (21)		CG (19)				
Outcome Variables	Before	After	Before	After	Before	After	YG—CG	YCG−CG	YG−YCG
Affective-cognitive depression	17.47 ± 7.55	12.84 ± 5.92*	14.86 ± 5.19	7.71 ± 3.31*	15.58 ± 7.37	18.32 ± 6.84*	.010 (-0.85)	<.001 (-1.97)	.014 (1.07)
Somatic depression	6.32 ± 1.83	3.68 ± 0.89*	5.19 ± 2.09	2.76 ± 1.14*	5.89 ± 2.05	5.63 ± 2.48	.002 (-1.04)	<.001 (-1.49)	.243 (0.9)
Depression	23.74 ± 9.01	17.32 ± 6.68*	20.05 ± 5.53	11.19 ± 3.97*	21.47 ± 8.8	24.79 ± 8.2*	.002 (-0.99)	<.001 (-2.11)	.012 (1.11)
Psychic anxiety	12 ± 3.22	7.79 ± 2.04*	11.48 ± 3.67	6.29 ± 1.71*	11.05 ± 3.82	11.95 ± 3.99ξ	<.001 (-1.31)	<.001 (-1.84)	.266 (0.79)
Somatic anxiety	11.26 ± 4.33	8.32 ± 3.09*	10.19 ± 4.36	6.57 ± 2.44*	10.37 ± 5.59	12.47 ± 5.04*	.003 (-0.99)	<.001 (-1.49)	.373 (0.62)

(Table 3 continued)

(Table 3 continued)

	Within Group Effects						Between Group Effects *P*-Value (Effect Size)		
	YG (19)		YCG (21)		CG (19)				
Outcome Variables	Before	After	Before	After	Before	After	YG—CG	YCG−CG	YG−YCG
Behavioral anxiety	1.63 ± 0.89	1.05 ± 0.52*	1.29 ± 0.96	0.9 ± 0.77*	1.42 ± 0.9	1.79 ± 1.03□	.019 (-0.9)	.003 (-0.97)	1.00 (0.22)
Anxiety	24.89 ± 7.11	17.16 ± 4.73*	22.95 ± 7.32	13.76 ± 3.89*	22.84 ± 8.6	26.21 ± 8.45*	<.001 (-1.32)	<.001 (-1.89)	.232 (0.78)
Intrusion PTSD	18.63 ± 4.35	14.32 ± 3.42*	18.38 ± 2.84	14 ± 1.98*	18.05 ± 4.65	19 ± 5.19ξ	<.001 (-1.06)	<.001 (-1.27)	1.00 (0.11)
Avoidance PTSD	7.16 ± 1.98	5.58 ± 1.35*	7.76 ± 2.21	5.71 ± 1.1*	7.37 ± 2.09	7.37 ± 2.09	.002 (-1.01)	.004 (-0.99)	1.00 (-0.10)
Numbing PTSD	17.89 ± 2.81	13.84 ± 2.39*	18.86 ± 3.14	14.57 ± 2.84*	18.95 ± 4.92	19.58 ± 5.49	<.001 (-1.35)	<.001 (-1.14)	1.00 (-0.28)
Hyperarousal PTSD	18.05 ± 3.12	14.32 ± 2.54*	18.81 ± 2.94	14.19 ± 2.58*	20.42 ± 5.14	22.84 ± 5.41*	<.001 (-2.01)	<.001 (-2.04)	1.00 (0.05)
PTSD	61.89 ± 9.52	48.05 ± 7.74*	63.76 ± 7.4	48.43 ± 6.59*	64.79 ± 14.07	68.79 ± 14.28*	<.001 (-1.8)	<.001 (-1.83)	1.00 (-0.05)

Note: *$P < .001$; □$P < .01$; ξ$P < .05$.

Abbreviations: YG, Yoga group; YCG, Yoga and concoction group; CG, control group; PTSD, posttraumatic stress disorder.

Table 4. Intergroup Comparisons Regarding Post QoL.

Outcomes	Compared Groups	Test Statistic	Standard Test Statistic (z)	*P-Value*	Effect Size (*r*)
Overall QoL	YG–CG	8.816	1.757	.24	0.28
	YCG–CG	11.395	2.326	.060	0.37
	YCG–YG	2.579	0.527	.99	0.08
General health	YG–CG	19.237	3.882	.001	0.63
	YCG–CG	23.112	4.780	.001	0.76
	YCG–YG	3.875	0.801	.99	0.13
Physical health	YG–CG	24.395	4.399	.001	0.71
	YCG–CG	31.679	5.854	.001	0.93
	YCG–YG	7.284	1.346	.54	0.21
Psychological health	YG–CG	10.184	1.849	.193	0.30
	YCG–CG	22.208	4.132	.001	0.65
	YCG–YG	12.024	2.237	.076	0.35
Social relations	YG–CG	1.553	0.283	.99	0.05
	YCG–CG	3.845	0.718	.99	0.11
	YCG–YG	2.292	0.428	.99	0.06
Environment	YG–CG	18.5	3.34	.003	0.54
	YCG–CG	10.618	1.964	.15	0.31
	YCG–YG	7.882	1.458	.43	0.23

Note: $P < .05$ is considered significant.

Abbreviations: YG, Yoga group; YCG, Yoga and concoction group; CG, control group; QoL, quality of life.

Table 5. Intragroup Comparisons on QoL.

	YG (n = 19)				YCG (n = 21)				CG (n = 19)			
	Mdn		z	r	Mdn		Z	R	Mdn		z	R
Outcome	Pre	Post	–	–	Pre	Post	–	–	Pre	Post	–	–
Overall QoL	3	3	-3.162□	-0.51	3	3	-3.755*	-0.58	3	3	-2.0ξ	-0.33
General health	2	3	-3.606*	-0.59	2	3	-3.945*	-0.608	3	2	-2.236ξ	-0.36
Physical health	10.86	13.71	-3.847*	-0.62	10.29	14.86	-4.021*	-0.62	11.43	10.86	-2.484ξ	-0.403
Psychological health	10.0	12.67	-3.856*	-0.63	10.67	13.34	-3.935*	-0.607	12.0	11.34	-3.380□	-0.55
Social relations	10.67	12.0	-2.877□	-0.47	10.67	12.0	-2.877□	-0.44	12.0	12.0	-2.209ξ	-0.35
Environment	11.5	12.5	-3.642*	-0.59	11.0	11.5	-3.341□	-0.52	11.0	10.5	-3.236□	-0.53

Note: *P < .001; □P < .01; ξP < .05.

Abbreviations: Mdn, median; QoL, quality of life.

Discussion

This study aimed to assess the independent and combined effect of OYI with Ayurvedic concoction on COVID-19-induced depression, anxiety, PTSD, and QoL. Both treatment conditions, i.e., 1-month OYI administered independently and jointly with Ayurvedic concoction, were effective in improving COVID-19-induced depression, anxiety, PTSD, and poor QoL. However, the synergistic effects of OYI and Ayurvedic concoction on depression, anxiety, PTSD, and QoL were higher than the independent effects of OYI except for the environmental factor of QoL. The result of the concoction seemed insignificant to improve QoL-related environmental settings and perceptions. The interactive effects of group and time (GxT) were higher than the independent effects of group (G) and time (T) on depression, anxiety, and PTSD. The depression-related affective-cognitive symptoms were improved more than somatic symptoms. The statistically significant improvements in anxiety-related factors—psychic, somatic, and behavioral and PTSD-related factors—hyperarousal, intrusion, numbing, and avoidance, were in descending order. The more psychic effect of Yoga and the somatic impact of Ayurveda intervention are well discussed in the classical texts. The behavior-related anxiety symptoms could not be well moderated by the short-term effects of administered OYI and OYAI. The OYI and OYAI also had an insignificant impact on environmental settings, things, and status related to QoL. However, significant restructuring of environment-related perceptions of the participants might be plausible by the effect of OYI rather than an Ayurvedic concoction.

The administered practice of commencing prayers and LES, SS, alligator twists, and other Yoga poses might be effective in alleviating psychosomatic symptoms and markers of post-COVID-19 depression, anxiety, PTSD, and health-related facets of QoL. Prior studies with consistent postural interventions have reported significant improvement in psychosomatic symptoms and markers of neuropsychiatric problems. The 90-min practice of yogic LES synchronized with deep breathing and mental awareness induces two important antimicrobial peptides—β-defensin and human-β-defensin-2 in respiratory epithelial cells during SARS-Cov-2 infection.[20] These practices also decrease joint stiffness and muscle spasm by enhancing synovial fluid secretion and range of motion. The effects of 12-week Yoga and meditation-based lifestyle, including Yoga poses—LES, warm-up, SN, supine, prone, sitting, standing; breath regulations and Omkar meditation significantly improved neuroplasticity (increased BDNF), mind–body communications (decreased cortisol, IL-6; increased sirtuin 1 and dehydroepiandrosterone sulfate), and cellular health (reduced reactive oxygen species and 8OH2dG, increased total antioxidant capacity and telomere activity) among the practitioners with the MDD as compared to their controls.[22] The 3-month practice of Hatha yogic postures, breath regulations, and Omkar meditation increased plasma melatonin and improved cardiorespiratory performance and psychological profile (anxiety, depression, and well-being).[21] Increased plasma melatonin by the effect of TM and combined practice of Hatha Yoga poses and Omkar meditation may act as antiviral, anti-inflammatory, immunomodulatory, antioxidant, and anti-infectious agents in visceral organs, brain, heart, bone, muscle, and skin.[20,21,61] Twelve-week Iyengar Yoga intervention, including postural and coherent breathing each for 15 min a day paced by an audio file, significantly increased the thalamic GABA level and decreased depression scores of the practitioners with MDD.[23,24]

Yogic breath regulations—UNB, ANB, HFYB, FDB, CB, coherent, and RB, included in OYI, have effectively ameliorated post-COVID-19 depression, anxiety, PTSD, and QoL. The 10-week practice of UNB by poststroke individuals effectively reduced their anxiety and increased language performance.[62] Right nostril Yoga breathing (RNYB) caused more oxygenated blood flow in the left prefrontal cortex than left nostril Yoga breathing (LNYB) and breath awareness (BA).[63] LNYB-induced volar galvanic skin resistance (GSR)

by implying the possible effects of RNYB on sympathetic upregulation, LNYB on sympathetic downregulation, and ANB on parasympathetic stimulation.[64] ANB reduces the systolic, diastolic, and mean BP indicative of low sympathetic tone.[65] ANB decreased relative power in the theta band during the practice and decreased postpractice beta amplitude, indicative of stress and anxiety management.[66] Coherent and FDB initiate adequate interhemispheric synchronization and generate a dominant global brain rhythm with high-frequency cerebral activity by downregulating the HPA axis and the sympathetic tone, resulting in improved autonomic and emotional control, cognitive functions, and the QoL.[67,68] FDB infuses 5 to 6 times more air into the lungs resulting in the optimal gaseous exchange between alveoli and pulmonary capillaries and enhanced elasticity and vascular supply to the lung tissues that remain passive during quiet breathing.[69] The 4-week practice of FDB preceded by 5-min LES cum preparatory poses reduced anxiety and negative affect and increased positive affect by modulating activity and connectivity of the emotion-processing brain sites—the amygdala, anterior cingulate, anterior insula, and the prefrontal cortex.[70] The CB, similar to Moorcha Pranayam as described in Hatha Yoga Pradipika, pacifies mental distractions, reduces sensory awareness, and induces a meditative mind indicative of remission of anxiety, depression, and PTSD.[71] RB practiced with Khechari, Shanmukhi Mudras, mental visualization, and external–internal breath retentions may increase CO_2 levels and 15 times more endogenous NO than quiet exhalation.[72] Elevated NO and CO_2 act as anti-inflammatory and antimicrobial agents to overcome the infection, relax bronchial tree smooth muscles, and improve the ventilation–perfusion ratio and breathlessness.[73]

The practice of PL and EASL stimulates external anal sphincter (EAS), ischiocavernosus, bulbospongiosus, transverse perineal muscles, the urethral sphincter, and the pelvic diaphragm,[74] especially pudendal nerve fibers to set the parasympathetic tone.[75] Interestingly, fMRI recorded multifocal cerebral cortical control areas and brain activities at anterior cingulate, prefrontal, parietal, occipital, and insular regions during sustained willful contraction of EAS (for 10 s)[76] are indicative of optimizing neuroendocrine secretions, neuronal functions, and improving depression, anxiety, PTSD, and impaired QoL.[75]

Dropping the chin into the sternal notch during TL stimulates baroreceptors in the carotid sinuses and interfers with the blood flow through the vertebral arteries resulting in lowered heart rate, stroke volume, and blood pressure.[77] AL practiced with inner breath retention increases the intra-abdominal pressure like a PL and Valsalva maneuver.[78] The tight squeezing of the lungs during AL induces excessive gas exchange between alveoli and pulmonary capillaries and enhances postpractice vascular supply to the gut.[79] The brief intermittent hypoxia developed during AL practice with outer breath retention might induce recombinant biochemicals and set novel physiological cascade—erythropoietin, vascular endothelial growth factors, nitric oxide synthase, p53 gene, stem cells migration, and histological resistance to diverse insults/injuries.[80] This indicates AL's plausible benefits in healing neuropsychiatric problems, anemia, hypertension, and lung tissues injured by SARS-Cov-2 infection.

The 20-min practice of SM preceded by 24 Gayatri Mantra recitations, proceeded with attentive visualization of rising solar rays penetrating the navel, heart, and crown chakras and concluded by recitations of five Omkar and Vedic prayers of physical, subtle and causal bodies [45] might be effective to moderate post-COVID-19 depression, anxiety, PTSD, and impaired QoL. Three-month Isha Yoga (including meditation: Samyama, Shoonya, Linga Sanchalan; Mantra repetition, body sensation visualization; and postural and BA practices) consistently increased the plasma BDNF level and mindfulness and decreased self-reported anxiety and depression.[81] Three-month TM practice decreased the perceived depression, anxiety, and stress negatively associated with T1–T2 changes in functional connectivity among posterior cingulate cortex (PCC), precuneus, and left superior parietal lobule and increased connectivity between PCC and right insula.[82] The 30-min practice of TM significantly increased serotonin metabolism (5-hydroxy indole-3-acetic acid) and decreased catecholamine metabolite, i.e., vanillic-mandelic acid, in experienced TM practitioners compared with their controls.[83]

The extracts—withanone, withanoside, and somniferine from *Withania somnifera,* tincordiside from *Tinospora cordifolia,* and vicenin, isorientin 4′-O-glucoside 2″-O-p-hydroxybenzoagte, ursolic acid, and scutellarin from *Ocimum tenuiflorum* inhibit entry and progression of SARS-Cov-2 into the human host cell.[39,84] Seven-day intake of an Ayurvedic formulation—Giloy, Tulsi, and Ashwagandha tablets, Swasari Vati, and Anu Taila with SC more significantly reduced the cascade of inflammatory markers—IL-6 and TNF-α and high sensitive-CRP of COVID-19 patients compared to their placebo controls.[16] The vital bioactive compounds—vitamins (C, K, E, β-carotene, and lycopene), polyunsaturated fats (linolic acid and alpha-linolenic acid), essential amino acids (threonine, valine, methionine, leucine, lysine, tryptophan, isoleucine, and phenylalanine), sugars (glucose, fructose, and xylose), lipids (lecithin, β-sitosterol, campesterol, and stigmasterol), and minerals (N, Ca, K, Na, Mg, Cu, Fe, Zn, and Mn) of *Hippophaes rhamnoides* fruit behave as antimicrobial, antiviral, anti-inflammatory, antiatherosclerotic, hepatoprotective, antioxidant, immunomodulatory, neuroprotective, and rejuvenating agents.[33,34] Twelve-week intake of *Vitis vinifera* based-dietary supplement—*Cognigrape* (250mg/day), significantly improved the cognitive and neuropsychological profile of the eaters compared to their placebo controls.[38] Glycyrrhizin and other bioactive compounds in the root and stem of *Licorice* have been proven neuroprotective, antidepressant, and effective for PTSD remission.[35] The bioactive alkaloid—piperine, contained in *Piper nigrum L,* has shown antidepressive,

antidiarrheal, analgesic, and immunomodulatory pharmacotherapeutic effects.[36] The phytochemicals in *Zingiber officinal*—6-shogaol and 6-gingerol, have induced antiviral, anti-inflammatory, immunomodulatory, neuroprotective, anti-arthritic, antiasthmatic, and appetizing effects.[37]

Thus, the optimization of neuroendocrine secretions, vagal tone, cardiopulmonary, and immunological functions by the OYI, and inhibition of entry and progression of SARS-Cov-2 via downregulation of inflammatory markers and upregulation of immune power by the intake of Ayurvedic herbal concoction administered herein support their observed effects for significant improvement of COVID-19-induced depression, anxiety, PTSD, and impaired QoL.

Conclusion

Online integral Yoga intervention and optimal Ayurvedic herbal formulation could be a harmless adjunctive treatment option in hospitals, wellness, and healthcare centers for managing COVID-19 and neuropsychiatric comorbidities.

Limitations and Recommendations

The observed results might be confounded by uncontrolled extraneous factors—diet, medications, sociocultural context, lifestyle, and social support system of the study participants. The data generated using self-rating psychometric tools might be affected by response bias, instrument bias, stigma, and participants' fears and intent to hide facts.

Poor internet connectivity, electronic gadgets, and interface operating skills might disturb patients' attention, adherence to the intervention, and data.

Therefore, further RCTs with reasonable sample size, one more arm for independent Ayurveda intervention, adequate biological markers of COVID-19-induced depression, anxiety, PTSD, and poor QoL, and offline intervention in a controlled environment and close observation are warranted to derive more valid and reliable results.

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Statement of Ethics

The study was approved by the Institutional Ethics Committee of the University of Patanjali (Ref. No.: UOP/IEC/2021/01) and registered in Clinical Trials Registry-India (CTRI/2021/05/033793).

Declaration of Conflicting Interests

The author declares no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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