Impact of Yoga and Meditation on Immune System – A Systematic Review and Meta-Analysis

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KEYWORDS
Yoga, meditation, immune system, mind body therapies.

ABSTRACT

Background: Yoga and Meditation is a mind body technique which has various positive effects on immune system and helps in bring down the inflammatory markers. Therefore, therapies based on Yoga and Meditation showed promising effects on immuno-compromised condition like HIV, Aim: To examine the effects of Yoga and Meditation on immune system functioning in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting systematic reviews.

Methods: Four electronic databases (MEDLINE/PubMed, Scopus, the Cochrane Central Register of Controlled Trials, and IndMED) were searched and the extraction of the applicable variables and assessing the risk of bias from the gathered studies was noted. The data analysis was done using, Review Manager software (RevMan; version 5.3.5) and R statistical software (version 3.6.1). Mean differences (MD), and standardize mean difference (SMD) were measured for continuous outcomes. Heterogeneity with the help of I2 statistic was used for the assessment of inconsistency across studies with the level of significance at P< 0.10. Publication bias was assessed using funnel plots, Egger's test for the selected studies.

Results:From a total of 141 papers, duplicates and other filtrations like languages other than English, non-clinical trials and non-RCT papers were excluded and finally 91 papers were selected for the present study. After the complete review of the selected papers, articles were grouped based on each immune parameters like Nuclear factor-kB , Interleukin-1b, Interleukin-6 , Tumor necrosis factor , CD4 T-cells, CD8-cells and NK cells. According to the inclusion and exclusion criteria, a total of nineteen RCTs were included in the meta-analysis.

Conclusion: Yoga may have potential for the supplemental treatment and prevention of inflammation-related disorders, according to current studies. Yoga practice may be beneficial as it combines the positive effects of physical activity with those of mindfulness; consequently, more research into the advantages of yoga-based therapies is especially important.

Systematic review registration: PROSPERO registration number- CRD42020187532

1. Introduction

Yoga is a mind–body medicine technique that is accepted to have health benefits in a variety of clinical and non-clinical conditions (1). Meditation is one of the component or branch of yoga practice which is primarily acting on the mind by improving the attention and awareness of the inner self and outer world, thereby reducing the psychological condition causing immune suppression, (2) The practice of yoga and meditation has been found to reduce IL-6, TNF-alpha, NF-kappa B and IL-1beta levels in breast cancer patients with increase in anti-inflammatory receptors. (3, 4) Yoga and meditation have been shown to increase IgA in pregnant women, providing a protection against the invading pathogens (5) and CD4 cells in HIV-infected individuals (6). Similarly, in healthy individuals, yoga and meditation technique significantly increases the IL-12, INF-gamma and serotonin with significant decrease in the adrenalin (7).

In developing and developed countries, chronic inflammatory diseases are found in large numbers due to the breakdown of immunoregulation system. The immune system develops on exposure to the microbes and works in a network balancing the production of anti-inflammatory and pro inflammatory markers. The immunoregulatory system in turn temporarily downregulates the immune response when its action is not required. During the acute or chronic condition, the immune regulation becomes the greater task for the immune system and the failure in this process, destruct the own cells and increase the inflammatory markers. Which lead to psychosomatic disorders and other disorders in individuals with increased risk. (8,9,10) The existing evidence

suggests that yoga can down regulate pro-inflammatory markers. (11) In particular, the qualitative evaluation of previous RCTs have revealed decrease in IL- 1beta, as well as indications for reductions in IL-6 and TNF-alpha. (12,13)

The present covid pandemic situation due to the human coronavirus (SARSCoV-2) infection presenting with complaints of fever, shortness of breath, mild to severe cold and other respiratory diseases. (14,15) The impact of the SARSCoV-2 in the human body leads to an increased IgA and IgM during the first week of exposure. In comparison to the IgM, IgA was found in large number which was helpful in managing further treatment procedures. (16)

The Covid-19 infected cells produce C-X-C motif chemokine ligand 10 in response to interferon gamma, which increases the pooling of inflammatory cells at the site of action causing inflammation (17). In Covid-19 patients diffuse alveolar damage with airway inflammation was found due to the virus load (18). The probable SARSCoV-2 binding to the epithelial cells of nasal cavity using the ACE2 receptor could be the reason for bronchopneumonia or other lung damages causing increased count of macrophages (17,18). Similarly, macrophages were found in abundance in the spleen and lymph node of Covid-19 cases. The infected macrophages further worsen the inflammation by producing large number of Interleukin 6 (IL6) which reduce the lymphocytes count and progress the tissue damage and lymphocytopenia (19).

The hyper response of the immune system led to increase in inflammatory action causing high infiltration of interferons, interleukins, tumor necrosis factor etc., ending with cytokine storm which was observed in the blood samples of severe covid positive patients (20).

This systematic review and meta-analysis will summarize the findings of randomized controlled trials examining the effects of yoga and meditation on immune system functioning which is essential to justify its application in the clinical treatment of emergency pandemic situation like COVID 19 scenario. The existing evidence suggests that yoga can down regulate pro-inflammatory markers (11). In particular, the qualitative evaluation of previous RCTs have revealed decrease in IL- 1beta, as well as indications for reductions in IL-6 and TNF-alpha (12,13).

Earlier study results imply that yoga may be applied as a complementary intervention for populations at risk or already suffering from diseases with an inflammatory component (21). Beyond this, yoga practice may give further beneficial effects by enhancing cell-mediated and mucosal immunity (6). It is hypothesized that longer duration and consistent practice of yoga and meditation are required to bring changes on circulating inflammatory markers.

Overall, this field of investigation is still under study, hence the current body of evidence is inadequate and for most immune parameters, more research is required to draw clear conclusions. The application of this meta-analysis will help the researchers to develop yoga module and give insight on research work benefitting the immune system.

The current systematic review and meta-analysis study will give in-depth scientific insight on the benefits of yoga and meditation on immune system

2. Methods

A comprehensive review of available controlled trial evidence to evaluate the effects of yoga and meditation on the immune system, markers of inflammation and anti-viral related immune responses was done (PROSPERO registration number: CRD42020187532). After the identification and developing of review objectives, eligibility criteria and search strategy were set. Final records were screened and analysis was done.

Search strategy

Using the PubMed, Google Scholar and, the Cochrane databases, research papers related to the Yoga and Meditation on Immune System published on or before June 2022 were collected. The search process was done based on the MeSH terms and key words such as “Immune system” OR “Yoga” OR “Meditation” OR “Mind body medicine” OR “Pranayama” OR “Relaxation technique” OR “Complementary therapies” AND “Interleukin” OR “Tumor Necrosis Factor” OR “Natural Killer Cells” OR “Activation Protein 1” OR “NF-kB” OR “CD 4,8” OR “CD cells” OR “Interleukins” OR “Immune System”.

Study Selection and data extraction:

Randomised controlled trials (RCTs), randomized cross-over studies and cluster-randomised trials were eligible

with no language restrictions applied for the inclusion. Studies were considered eligible, if they had at least one of the primary outcomes- Nuclear factor-kB (NF-kB) A, Activator protein 1 (AP1), Interleukin-1b (IL-1B), Interleukin-6 (IL-6),Tumor necrosis factor (TNF),CD4 T-cells and CD8 T cells and NK cells.

The abstracts of the articles were screened and selected independently by the reviewers, and potentially eligible articles were read in full by two reviewers. Disagreements were settled through a discussion with a third reviewer until consensus was reached. If necessary, additional information was obtained from the authors of the primary study.

Data analysis

Assessment of overall effect size

Meta-analyses were conducted using metafor package in R statistical software version 4.0.2. In order to be able to perform a meta-analysis on a specific outcome, at least two RCTs had to have assessed one of the primary outcomes (i.e. if a specific outcome is assessed in only one RCT, no meta-analysis is performed; if it is assessed by two or more RCTs, a meta-analysis will be performed). Separate analyses were conducted for comparisons of yoga to different control interventions. For dichotomous outcomes, odds ratios (OR) with 95% confidence intervals (CIs) was calculated. For continuous outcomes, standardized mean differences (SMDs) with 95% CIs was calculated as the difference in means between groups, divided by the pooled standard deviation, using Hedges' correction for small study samples. Where no standard deviations were available, they were calculated from standard errors, CIs or t-values, or attempts were made to obtain the missing data from the studies' authors by email.

Assessment of heterogeneity

The I^2 statistic was be used in order to analyse the statistical heterogeneity between the studies. The magnitude of heterogeneity was categorised as I^2= 0–24% being low, I2=25–49% being moderate, I2 =50–74% being substantial and I2=75– 100% being considerable heterogeneity. The $\chi 2$ test was further used in order to assess whether differences in results were compatible with chance alone. Given the low power of this test, when only few studies or studies with low sample sizes were included in a meta-analysis, a p-value = 0.10 was regarded as indicating significant heterogeneity.

Assessment of risk of bias

Risk of bias was assessed independently by two reviewers using the Cochrane risk of bias tool. This tool assesses the risk of bias on seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. For each domain, risk of bias was assessed as low, unclear or high. Disagreements were settled through discussion with a third reviewer until consensus was achieved.

3. Results

Study selection and data extraction

From total 141 papers, duplicates and other filtrations like languages other than English, non- clinical trials and non-RCT papers were excluded and finally 91 papers were selected for the present study. After the complete review of the selected papers, articles were grouped based each immune parameters like Nuclear factor-kB (NF-kB) A, Interleukin-1b (IL-1B), Interleukin-6 (IL-6), Tumor necrosis factor (TNF), CD4 T-cells, CD8-cells and NK cells. The data extracted from the finalized papers were Author name with year, total number, Mean, standard deviation of experiment and control group. According to the inclusion and exclusion criteria, a total of nineteen RCTs were included in the meta-analysis. The PRISMA flow diagram of the studies is given in figure 1 and characteristics of the studies in table 1.

Table: 1- Characteristics of the included studies

S.no	Author	Year	Duration of intervention	Type of intervention	Frequency of intervention
1	Jirakrit Leelarungrayub(22)	2020	30 days	fast deep breathing	30 breaths in three sets, with 2- to 3-minute intervals for rest twice daily, morning and evening
2	Paula R. Pullen, Med, (23)	2008	8 weeks duration of 70 mins	Yoga sessions .	twice per week, for a total of 16 sessions over 8 weeks duration of 70 mins

3	Waleed O. Twal (24)	2016	immediate effect- 20 mins single session	Yogic breathing	10 min of Om chanting (Pranava Pranayama) followed by 10 min of TMP- the participants were taught to inhale through one nostril for two counts, hold the breath for eight counts, and exhale for four counts. This cycle was repeated for 10 min. totaly twenty minutes in a single session
4	Raj Kumar Yadav (25)	2012	10 days	asanas (postures), pranayama (breathing exercises), stress management, group discussions, lectures, and individualized advice	2hrs each day
5	M. Ernberg (26)	2018	15 wks	Resistance exercise	10 min bicy cling to warm up and was then followed by a 50 min strength training protocol. Twice per week during 15 weeks
6	KN Harkess (27)	2016	8 wks	Yoga intervention	twice-weekly, hour-long yoga classes (the total number of classes offered was 16
7	Kyung Bong Koh (28)	2008	4 weeks	Relaxation Training	relaxation training- 60 min one week prior to the study, and two such sessions by one senior psychiatrist. relaxation procedure on their own twice (between 6:00 and 6:30 a.m. and between 6:00 and 6:30 p.m.) a day for at least 15 min each day.
8	Neng Chen, (29)	2016	8 wk	Hatha yoga (60 mins): breathing exercise (6 mins); loosening exercise(i.e., corn tree pose) (10 mins); standing poses (i.e., warrior pose and mountain pose) (8 mins); supineposes (i.e., bridge pose and dolphin plank pose) (8 mins); prone poses (i.e., hare pose and locust pose) (8 mins); sitting poses (i.e., staff pose and hero pose) (8 mins); relaxation/corpse pose (6 mins); and seated meditation (6 mins). Approximately 32 minutes is spent in active poses.	60 min per session (2 times/wk) for a total of 16 times
9	Aleksandra E. Zgierska (30)	2016	26 wks	mindfulness meditation and cognitive behavioral therapy (CBT)	eight weekly group sessions.6 days per week for at least 30minutes per day at home- 26 wks
10	Frederick M. Hecht (31)	2018	3 months and follow up 12 months	mindfulness-based stress reduction (MBSR)	eight weekly classes of 2.5 hours duration. 8-hour silent retreat during the sixth week of the program; and assignments for home practice. includes body scan meditation, gentle yoga focused on body awareness, sitting meditation, 45 minutes per day of meditation and yoga practice 6 days per week
11	Abilio Reig-Ferrer (32)	2014	2-week intervention period and a 3-month follow-up period.	relaxation technique based on Benson's relaxation	Hour-long group sessions were conducted daily, from Monday through Friday, for a total of 10 days in a span of two weeks.
12	WT Cade, (33)	2010	Ashtanga Vinyasa yoga- held two or three times per week for 60 min per session and participants were enrolled for 20 weeks.	Ashtanga Vinyasa yoga	60 min per session and participants were enrolled for 20 weeks.
13	J. David Creswell (34)	2009	8 wks	Mindfulness- based stress reduction (MBSR)	8-week Mindfulness- based stress reduction (MBSR)- included eight weekly 120-min group sessions,a day-long retreat in the seventh week,and 30MINS daily home mindfulness meditation practice.

14	Elizabeth A. Hoge (35)	2017	8 wks	MBSR	MBSR is an 8-week group-based intervention with a single weekend "retreat" day and daily home practice guided by audio recordings. I
15	Janice K. Kiecolt-Glaser (36)	2014	12 weeks of 90-minute, twice per week hatha yoga classes	hatha yoga classes	90-minute, twice per week
16	Barry S. Oken (37)	2010	7 WK	mindfull meditation	interventions lasted 7 weeks, and consisted of one 90-minute session per week along with at-home implementation of knowledge learned.
17	Selvakumar Ganesan (38)	2020	12 weeks.	YG for 12 weeks, along with standard medical treatment.	30 min, 3 times/week- 12 wks
18	Linda E. Carlson a, (39)	2007	8 WKS	eight-week MBSR program that incorporated relaxation, meditation, gentle yoga and daily home practice.	The intervention was provided over the course of eight weekly, 90-min group sessions with a maximum of 15 participants each, plus a 3-h silent retreat on the Saturday between weeks six and seven.
19	Traci McArdle, and John Carpenter, (40)	2017	eight weekly sessions of CBSM and moderate-intensity aerobic exercise three times per week	CBSM and moderate-intensity aerobic exercise	8wks, 4month and 10 month

Meta Effect of Yoga and Meditation on CD 4 level

The random meta effect of different yoga and meditation is found effective to decrease CD4 by 0.16 standard deviation unit (SMD= -0.16, 95%CI= [-0.44, 0.11], I^2=0%, P=0.49) compared to placebo control or placebo cum standard control. The 95% CI, including a null effect line, shows a statistically insignificant meta effect of Yoga and Meditation on CD 4 level with no more precision. I^2 0% indicates no variation between observed and expected effects of Yoga and Meditation on CD 4 level in the five included studies (Fig 2).

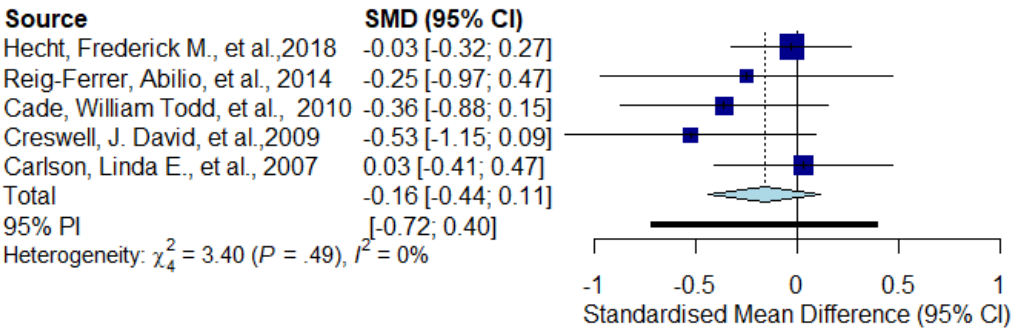

Figure: 2- Forest plot for CD4

Meta Effect of Yoga and Meditation on TNF alpha level

The random meta effect of different yoga and meditation is found effective to increase TNF alpha by 0.68 standard deviation unit (SMD= 0.68, 95%CI= [-0.04, 1.40], I^2=96%, P=0.001) compared to placebo control or placebo cum standard control. The 95% CI, including a null effect line, shows a statistically insignificant meta effect of Yoga and Meditation on TNF alpha with no more precision. I^2 96% indicates high level of heterogenicity between observed and expected effects of Yoga and Meditation on TNF alpha in the ten included studies (Fig 3).

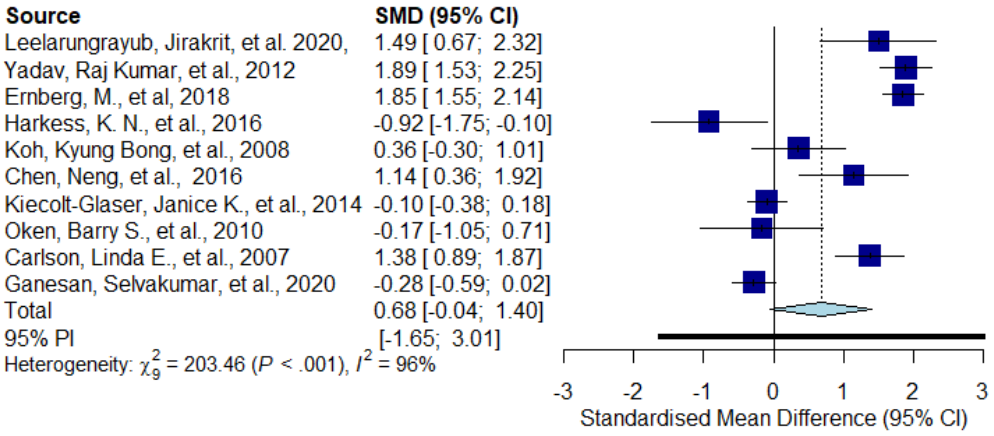

Figure: 3- Forest plot for TNF alpha

Meta Effect of Yoga and Meditation on IL-1b level

The random meta effect of different yoga and meditation is found effective to decrease IL-1b alpha by 0.22 standard deviation unit (SMD= -0.22, 95%CI= [-1.00, 0.57], I^2=61%, P=0.05) compared to placebo control or placebo cum standard control. The 95% CI, including a null effect line, shows a statistically insignificant meta effect of Yoga and Meditation on IL-1b with no more precision. I^2 61% indicates moderate level of heterogenicity between observed and expected effects of Yoga and Meditation on IL-1b in the four included studies (Fig 4).

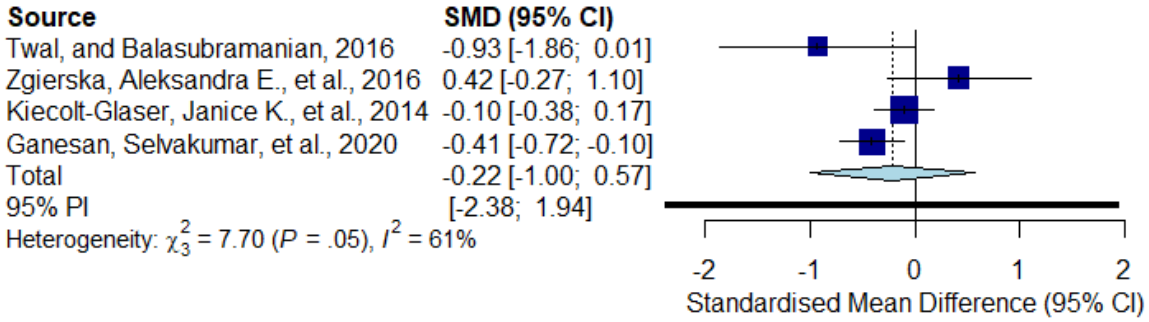

Figure: 4 - Forest plot for IL-B level

Meta Effect of Yoga and Meditation on IL-6 level

The random meta effect of different yoga and meditation is found effective to increase IL-6 by 0.24 standard deviation unit (SMD= 0.24, 95%CI= [-1.14, 0.62], I^2=66%, P=0.002) compared to placebo control or placebo cum standard control. The 95% CI, including a null effect line, shows a statistically insignificant meta effect of Yoga and Meditation on IL-6 with no more precision. I^2 96% indicates high level of heterogenicity between observed and expected effects of Yoga and Meditation on IL-6 in the ten included studies (Fig 5).

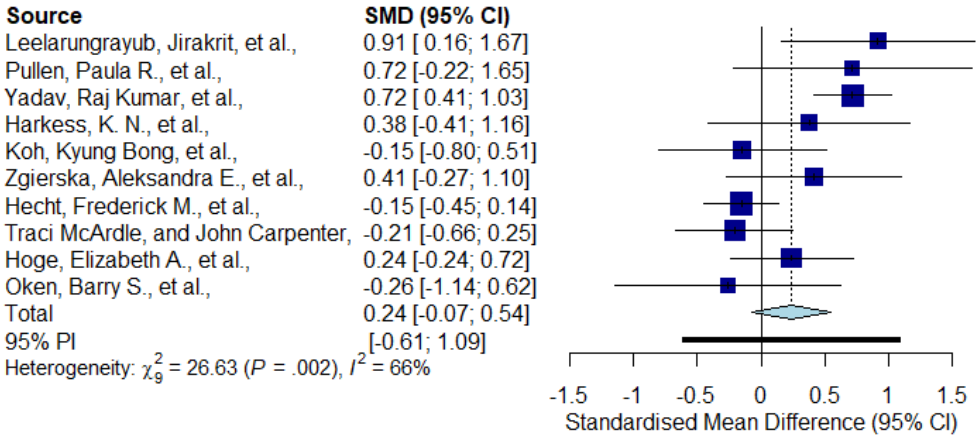

Figure: 5 - Forest plot for IL-6 level

4. Discussion

This is the first systematic review to summaries the findings of available RCTs investigating the impact of yoga on immune system functioning. The downregulation of pro-inflammatory markers is an overall pattern that can be identified in the effects of yoga on immunological functioning. In terms of cytokines and other circulating inflammatory markers, the most compelling evidence is that yoga practice reduces levels of the pro-inflammatory cytokine IL-1beta in both healthy and sick populations. Despite the fact that effect sizes were small to medium, this effect was unequivocally demonstrated by all research that evaluated this parameter.

Regarding the effects of yoga on IL-6, the evidence is less consistent. Half of the studies investigating this parameter indicated that yoga practice decreases IL-6 levels, with no directly opposing results. Effect sizes of these studies in our study showed controversial direction than the effect proposed by the included studies.

Concerning TNF-alpha, the existing studies report mixed results, currently impeding distinct conclusions. Yet, there are indications that yoga can increase levels of this inflammatory marker as well, and similar as for IL-6, no directly favoring results were found.

While the findings for CRP, TNF alpha, and IL-6 are not as conclusive as those for IL-1beta, a relationship between yoga practice and decreases in these markers would be consistent with decreases in IL-1beta. All of these indicators are major mediators of the inflammatory response, making them essential for proper immunological function. However, dysregulation or prolonged increase of any of these parameters can have negative consequences: IL-1beta is involved in the pathophysiology of inflammatory disorders such as rheumatoid arthritis, type 2 diabetes, and gout.

A meta-analysis investigating the effects of MBTs on different immune parameters concluded that MBTs reduce inflammation, mainly evidenced through reductions in CRP (41) .Yet, similar to our review, this study found inconsistent evidence regarding the effects of MBTs on different other circulating markers of inflammation.

Another systematic analysis indicated that mindfulness meditation can reduce CD4 + cell counts in HIV-infected persons in terms of immunological indicators other than inflammation (2) This discovery supports the findings of the Naoroibam et al. (6) , which revealed similar effects for yoga and was included in our review.

While yoga appears to have essentially the same effects on the immune system as other MBTs, it may offer certain advantages over other MBTs as well as exercise-based therapies. Yoga has been demonstrated to promote psychological well-being more than other MBTs such as sitting meditation (42) (Sauer-Zavala et al., have shown equivalent or superior effects on numerous health-related outcomes when compared to other exercise-based therapies (43). Yoga practice may be especially useful because it combines the positive effects of physical activity with those of mindfulness; consequently, more research into the advantages of yoga-based therapies is especially important.

5. Conclusion

Yoga may have potential for the supplemental treatment and prevention of inflammation-related disorders, according to current studies. However, the present information for several criteria is inconclusive or insufficient, prompting further research. It needs to be seen whether consistent benefits of yoga on circulating pro-inflammatory markers develop over prolonged periods of practice. Furthermore, the possibly beneficial benefits of yoga on other elements of immune functioning, such as cell-mediated immunity, need to be investigated further.

Study Impact :The study findings can be utilized for developing yoga module and will help in the implementation of yoga and meditation along with the pharmacological therapies in improving the immune status.

Study Application: This study will especially help in handling of emergency immunocompromised scenario like the current COVID 19 pandemic situation as yoga has several advantages because of its non-invasive character, and the absence of negative side effects.

Author contribution

Conceptualization: R.A , K.M ; Data curation and Analysis : R.A, K.M, T.S; Writing, Review and Editing: R.A, K.M, T.S.

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