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A Systematic Review Report on Impact of Yoga Practices on Immune Response with Special Reference to SARS-COV-2 Pandemic

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Abstract

The Pandemic of Covid-19 is wreaking havoc to healthcare systems all over the world. Although, no treatment has been approved till now. The aim of the present study is to summarize the existing evidence of RCT (random control trial) examining the effect of yoga on immune system. This will connect the traditional knowledge and clinical evidence together for future translation research on covid-19 prophylaxis. A systematic review was conducted as per the PRISMA guidelines. The search was conducted using Pub Med, Science direct and EMASE database for 2000 years. Search resulted 310 articles and finally 25 articles are included for systematic review.

The finding suggests that regular yoga practices boost the immune system by down regulating pro-inflammatory markers with increasing level of antibodies and anti-viral immune réponses.In conclusion, the study speculated yoga as a cost effective adjuvant for fighting against COVID-19.

Keywords: Corona; Yoga; COVID-19; Immune system; Inflammatory parameters; Antibodies.

INTRODUCTION

The novel Corona Virus Disease, is a kind of viral pneumonia, was arise from Wuhan city, China and was first reported to the WHO on December 31, 2019.[1,2] The new virus generally known as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2 virus) is very contagious and rapidly the epidemic has spread all over the world.[3] In March 2020, the World Health Organization (WHO) announced SARS-CoV-2 as a pandemic and eventually led to profound global health crisis. The COVID-19 outbreaks are proving to be an unprecedented challenge to healthcare systems all over the world.

COVID-19 belongs to beta corona virus family and has genomic sequence close to previous known SARS virus. Although, it represents the most prevalent and pathogenic forms of communicable infectious diseases. The Coronavirus S protein (spike protein) has a strong affinity to binds the human ACE-2 for their entry inside cells.[4,5] SARS-CoV-2 virus altered the host machinery and suppresses the body's immune response leading

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to severe acute respiratory illness and chronic inflammation.[6] The damaged cells induce innate inflammation and cytokine storms (IFN-α, IFN-γ, IL-1β, IL-6, IL-12, TNF-α etc.) and found to be the main death cause of COVID-19 patients.[7-9]

Due to absence of any approved drug and vaccine all over the world health care is confronted with a number of issues including huge disease burden, lack of adequate health infrastructure and manpower. Prevention is the best strategy to fight and reduce the severity of COVID-19. The health promotion activities like yoga and physical activity has discovered as potential preventive measure considering the lack of treatment with the mutual benefits of cost efficient, easy to apply in lockdown period. Recently, Yoga have received great interest as multidimensional behavioral and complementary therapies to strength the immune system, respiratory system, reducing stress in COVID-19 pandemic. In India continent, yoga has been used for enhancing immunity since Vedic period. Yoga practice including exercise (asanas), controlled breathing (pranayam), meditation, relaxation, and concentration.[10] Several studies have reported that the occurrence and development of SARS-CoV-2 depend on the interaction between the virus and the individual's immune system. In initial stage of infection weak innate and adaptive response allow entry of virus and leads the progression of mild infection to sever disease. Therefore, the foremost strategy towards the prevention of disease is to boost immune responses. Several studies reported the significant improving effect of yoga practices onimmune system through increasing the essential component of immune system such as macrophages, monocytes, neutrophils, immunoglobulin and T-lymphocytes.[10] It also boosts anti-viral immune responses, decrease markers of inflammation and stress. In addition, it improveslung functions and lower the risk of pneumonia and acute respiratory distress syndrome (ARDS) which are the common disorders develop with COVID-19. Yoga has received increasing awareness and attention from the scientific community seeking to understand the safety and health functioning benefits. The aim of the present study is to summarize the existing evidence of RCT (random control trial) examining the effect of yoga and meditation on immunological and inflammatory parameters. This will bridge the traditional knowledge and clinical evidence for future translation research for COVID-19 prophylaxis. Based on these findings, recommendations for future research are offered to fight against COVID-19 pandemic.

METHODS

Data study and Search Process: Literature search was performed using Pub Med, Science direct and EMASE database for articles published till 2000 years. Search term included corona virus, yoga and meditation, immune system, immunological parameters, cytokine, inflammation and antibodies. The search resulted 310 articles. Due to lack of RCT examine the effect of yoga on COVID-19 patients, authors included articles on RCT examine the effect of yoga on immune system for providing a summary of clinical experience to narrate its importance to fight against SARS-CoV-2 virus.

Included Criteria: The search limited to articles being published in English language. All the articles investigating the effect of yoga practices (yoga asana, breathing and meditation) in one of the immunological and inflammatory parameters are included in study (Fig. 1). No further limitation was made including participant type, timing, duration and type of yoga and meditation practices.

Data abstraction and quality assessment: Applying the aforementioned techniques, 310 studies were retrieved and considered for initial evaluation. First and second author independently extracted data from eligible publication with following details: participant characteristics, details of the intervention of yoga, type of control condition, type and timing of outcome assessment, and reported immune outcomes.

RESULTS AND DISCUSSION

The outbreaks of COVID-19 created a substantial public health challenge. The clinical studies examining the effect of yoga on COVID patients are in their infancy and have yet to be proved. Although, the indirect anti-viral activities has proven. Its anti-inflammatory, antioxidant and immune enhancing activity support its potential attenuation for Covid-19 infection. Due to the heterogeneity of the included studies, limited number of trials and the variation of participants, authors have not performed meta-analysis and only summarized and analyzed the studies (Table 1).

Table 1: Summary of studies evaluating the effect of yoga and meditation on Immunological parameters

Author	Sample size	Sample characteristic	Intervention type	Duration	Outcomes
Agnihotri et al. (2014)	Experimental group n =121; control group n = 120	Patients with mild to moderate asthma mean age 37.86	Yoga practice	30 in/session; 5 times/week; 6 months	Significant reduced in eosinophils in yoga group. No significant difference in total leukocyte count, polymorphs, monocytes and lymphocytes.
Black et al (2013)	Experimental group n = 23; Control group n = 16	healthy individuals confronting care giving stress; mean age 60.5 years	Kirtan Kriya Meditation (KKM)	8 weeks	Up-regulated the immunoglobulin -related transcripts genes and downregulated pro-inflammatory cytokines transcripts genes.
Bower et al. (2014)	Experimental group n = 14, control group n = 15	Breast cancer survivors; mean age 54 yr	Yoga practice	90 min/ session; 2 times/week; 12 weeks	Significantly lowered activity of NF-kappaB and activity of CREB family transcription factors, increased activity of anti-inflammatory glucocorticoid receptor in yoga group. No difference in sTNF-rII levels in yoga group but significantly increased in controls ; no significant difference in CRP , IL-1ra and IL-6 between-group.
Cade et al. (2010)	Experimental group n = 29; Control group n = 21	HIV-infected individuals mean age 45yr	Yoga practice	60 min/ session; 2–3 times/ week; 20 weeks;	No significant difference in CD4 + cell count between groups.
Chandwani, et al (2014)	Experimental group n = 53; Control group n = 53	women with breast cancer, 52.38	Yoga	three times a week for 6 weeks	Significant reduction in cortisol level
Chen et al. (2016)	Experimental group n = 15; Control group n = 15	Healthy individuals, ; mean age 18–25 years	Hatha yoga practice	60 min/ session; 2 times/week; 8 weeks	Significant reduction in TLR2receptor agonist stimulated levels of IL- 6, TNF-alpha and IL-1beta in yoga group ;significant reduction in LPS stimulated TNFalpha but no effect on LPS stimulated IL-6 and IL-1beta; no significant difference inIL-8, TNF-alpha.
Creswell et al (2009)	Experimental group n = 33; Control group n = 15	HIV infected adults; mean age 41	Meditation program	2hr daily, 8-week	Significant reduction in CD4+ T lymphocyte.
Creswell et al (2012)	Experimental group n = 20; control group n = 20	Healthy older adults, mean age 65(55-85yr)	Meditation	30 min of daily home mindfulness practice six days a week for 8 week	downregulated NF-κB-associated gene expression and CRP level; no significant difference in IL-6 .
Davidson et al (2003)	Experimental group n = 25; Control group n = 16	Adult with ulcerative colitis, mean age 36yr	Meditation	60mins, 6 times/week, 8 week	significant increases in antibody titers to influenza vaccine
Elsenbruch (2005)	Experimental group n = 15; Control group n = 15	Patients with ulcerative colitis (UC); mean age 43years	Mind-body therapy	6hr, 1 times/ week	no significant effects on TNF and circulating lymphocyte subsets, including T helper cells,cytotoxic/suppressor T cells , NK cells and monocytes

Fan et al (2010)	Experimental group n = 17; Control group n = 18	Healthy under graduate students; mean age 21yr	Meditation	20 mins, 7 times/week, 4 week	sIgA levels increased significantly.
Gopal et al. (2011)	Experimental group n = 30; Control group n = 30	Healthy students under examination stress	Yoga practice	35 min/ session; daily; 12 weeks	Significant decrease in IFN-gamma less pronounced in yoga group compared to controls; no significant difference in IL-4between group
Harkess et al. (2016)	Experimental group n = 11; Control group n = 15	Healthy individuals reporting psychological distress; mean age 41.21 yr	Yoga practice	60 min/ session; 2times/week; 8 weeks	No significant differences in CRP, IL-6 and TNFalpha between group.
Hidderleya and Holt, (2008)	Experimental group n = 16; Control group n = 17	Woman with early stage breast cancer, mean age 16-65yr	Meditation	8 week	Significant difference in the CD8 and the Natural Killer Cells. No significant difference in CD4 and B cell
Kiecolt-Glaser et al. (2014)	Experimental group n = 96; Control group n = 90	Breast cancer survivors; mean age 51.6 yr	Hatha yoga practice	90 min/ session; 2 times/week; 12 weeks;	Significant decrease in LPS stimulated IL-6, TNF-alpha, and IL-1beta at 3 months follow-up in yoga group; no significant differences between group immediately post intervention.
Lengacher et al (2013)	Experimental group n = 41; Control group n = 43	women with breast cancer treatment	MBSR	6-week	Significant increase in cell counts of both T and B cells, CD4þ cells
Lim and Cheong (2015)	Yoga group n = 12; control group n = 13	Healthy students inexperienced in yoga; 56% female; mean age 21.5 years	Yoga practice	90 min/ session, once/week; 12 weeks;	Significant increase in IL-12 and INF-gamma in yoga group compared to controls; no significant between-group difference in TNF-alpha
Naoroibam et al. (2016)	Yoga group n = 22; control group n = 22	HIV-infected individuals; 42% female; mean age 36.14 years	Yoga practice	60 min/ session, 6 times/week; 1 month	Significant increase in CD4 + cell count in yoga group compared to controls
Parma et al. (2015)	Yoga group n = 20; control group n = 26;	Breast cancer survivors; mean age 56.2 ± 7.9 years	Hatha yoga practice;	60 min/ session; 3 times/week; 6 months	No significant difference between yoga and both control groups for IL-6,IL-8 TNF-alpha and CRP
Pullen et al. (2010)	Experimental group n = 18; Control. group n = 16	Heart failure patients; mean age 54.23 years	Yoga practice and meditation	60 min/ session; 2times/week; 16 sessions over 8–10 weeks;	Significant reduction in IL-6 and CRP in yoga group.
Rao et al(2008)	Experimental group n = 33, control n = 36	Breast cancer patients pre and post operation ; mean age 49yr	Yoga practice	4 weeks	Significant lower levels of serum IgA in the yoga group; no significant difference in IgM and IgG levels.
Rajbhoj et al. (2015)	Experimental group n = 19; Control group n = 18	Industrial workers with increased risk of chronic; mean age 40.45 years	Yoga practice	45 min/ session; 6 times/week; 12 weeks	Significant decrease in IL-1beta and increase in IL-10 in yoga group.

Sharma et al. (2015)	Yoga group n = 44; control group n = 43	Patients with inflammatory bowel disease; Age range:16–60 years	Yoga practice	60 min/ session; daily for one week; 7 week	No significant difference in sIL-2r between group
Vogler et al. (2011)	Experimental group n = 19; Control group n = 19	Physically inactive older adults; mean age 73.21 yr	Yoga practice	90 min/ session, 2times/week, 8 weeks;	No significant between group difference in IgA level.
Subrama-nian et al (2012)	Experimental group n = 21; Control group n = 21	Undergraduate students under examination stress; age: 18-23 years.	Sudarshan kriya and Pranayam	six weeks	Significant reduction in neutrophils platelets, Lymphocyte count.

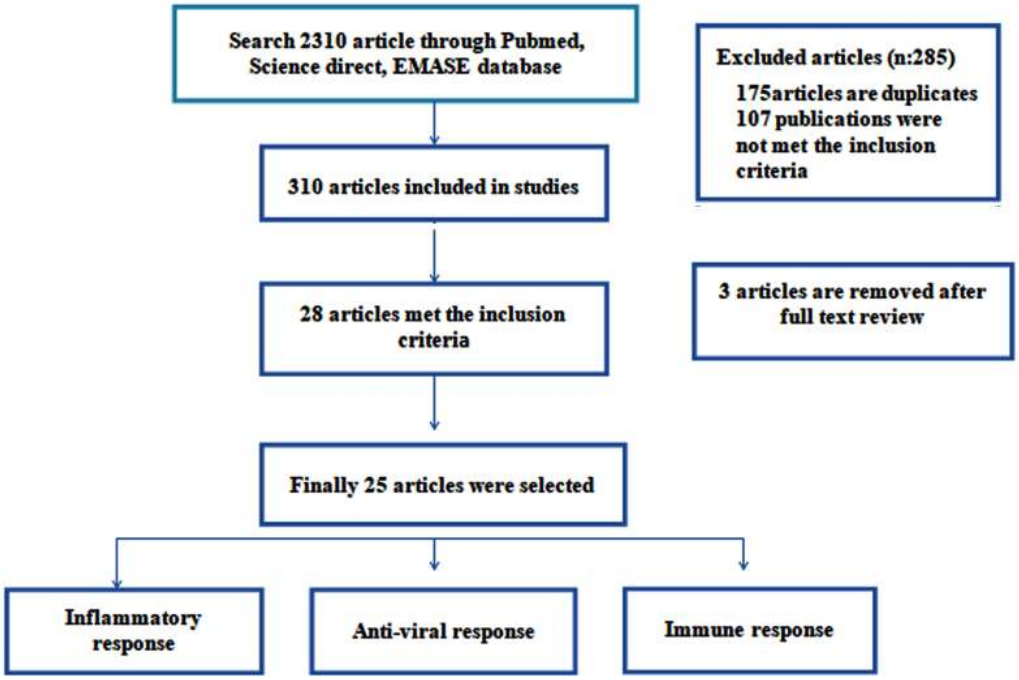

Fig. 1: Outline of data selection

Literature search

The fig. 1 illustrates the process of selecting articles in databases yielded 310 results during 2000. of these, 175 titles duplicates and 107 publications were not met the inclusion criteria and therefore, they were removed. In total, 28 full text articles were met the inclusion criteria for final review. Three articles were removed for different reasons. Finally 25 articles are included in study.

Characteristic of Studies

A total of 1498 participant were included in study to evaluate the effect of yoga on immune system. Mean sample sizes of most of the study are small (n-36). Three studies[11-13] examine the effect of yoga and meditation on medium sample size (n-92.3) and two studies[14,15] on large sample of mean size (213.5).

In total 25 studies included in the review process containing both clinical and non clinical population. There are 351 participants which are non clinical and 885 participants are clinical such as patients of breast cancer (n-351), HIV (n-142), ulcerative colitis (n-71), inflammatory bowel syndrome (n-87), heart failure.[34] Age of participant ranges from 12 yrs to 75 yrs. Duration of intervention ranges 1-7 days/week for 6 weeks to 6 months. In most of the studies, duration of intervention ranges 6-12 weeks except

two studies evaluated the effect after 5 months[16] and 6 months[15] of intervention.

Effects of yoga practice on markers of inflammation with special reference to COVID-19

The most critical characteristic of COVID-19 patients were "cytokine storms". Previous studies revealed the marked increase in pro-inflammatory markers includes; IL-1β, IL-6, IL-8, TNFα causes excessive inflammation and depressed immune system and substantially contribute the pathogenesis of COVID-19 infection. Therefore, attenuation of cytokine storm could be the foremost way to combat Covid-19.

The finding of the present study observed the moderate effect of yoga and meditation in reducing markers of pro-inflammatory especially IL-1, IL-6, IL-8 and TNFα and increasing anti-inflammatory includes IL-4, IL-10. Three studies[14,17,18] observed significant effect in reducing the IL-1 level in both clinical and non clinical population. The studies depict the effect of yoga on IL-6 level were inconsistent, although overall trend of yoga practice were towards the lowering the IL-6 level. In addition, Pollen et al.[17] and Kiecolt-Glaser et al[14] found robust effect of yoga on IL-6 level in heart failure patients and breast cancer survivors respectively. Out of two studies, no studies observed a significant effect on IL-8 in healthy and clinical patients both. One study analyzes sIL-2r which regulates processes of tolerance and immunity, although no significant difference observed between yoga and control group. Tumor necrosis factor (TNF) is the amplifier of inflammation and found elevated in COVID patients significantly. Our finding observed that most of the study examine the effect of yoga on small population except Kiecolt-Glaser et al[14] of mean size 186 and shown significant reduction in LPS stimulated TNF level in breast cancer survivors after 3 months not immediately post intervention. This implies that duration of intervention might have profound effect on response and proposed the sustain yoga practice for consistent and positive outcome. Bower et al19found increased activity of anti-inflammatory glucocorticoid receptor in yoga group which signifies higher GR activity and suppress pro-inflammatory genes. Our finding revealed that yoga practices down regulated pro-inflammatory gene expression which supports the previous studies advocating that yoga and meditation lower the production of stimulated pro-inflammatory cytokine.

Effects of yoga practice on anti-viral response with special reference to COVID-19

Interferon's (IFN) are the group of small protein secreted by various cell of immune system to protect the body from foreign matters.[5] When the virus entered in cell, IFN α and IFN β are the cytokines produced by virus infected cell to limit the virus replication and also modulate other component of innate and adaptive immune response such as natural killer cell (Nk), CD 8 T cells. Gamma interferon (IFN-gamma) is secreted by T cells, natural killer (NK) cells and macrophages to activate the immune system in respond to infectious agents. Our finding reported two studies explaining the effect of yoga practice in increasing the production of anti-viral cytokine IFNγ which directly inhibit viral replication and enhance antigen presentation.[20] Although, ongoing investigation found IFN α and IFN β more efficient to dissimilate corona virus infections at early stage.[21] Lim and Cheong[22] observed the significant increase in IL-12 in healthy individual in yoga group comparing to control. IL-12 play primary role in activation of innate immune response and is critical factor to develop immunity against virus infection. It have been reported that SARS-CoV-2 virus quite resemble to pneumonia virus and found to play important role in it. CRP considered as bio-marker of inflammation process and COVID-19 infection. It have been noticed that Covid-19 is the result of dysregulation in activation of complement system which is the immune surveillance system to eliminate the virus or any foreign agent. Four studies evaluated the effect of CRP level and only one study observed the significant reduction of CRP levels.[17]

Effects of yoga practice on immune response with special reference to COVID-19

Several studies showed the uncontrolled immune response due to the hyper activation of macrophages and monocytes in Covid-19 patients. This response results in an increase in neutrophils, reactive protein C (CPR) and in decrease in the total number of lymphocytes antibodies. Our finding revealed that mediation has robust effect on monocyte, neutrophiles and other circulating lymphocyte subsets such as helper T cell, NK cells. In Severe COVID 19 patients observed a marked reduction in both T cells and Nk cell and eventually secondary lymphoid tissues had been destroyed. More than of 80-90% critical patients are associated with leukopenia with severe lymphopenia involving a dramatic loss of CD4+ T cells and CD 8 T cells. It have been also reported that severity

of disease is correlated with lymphocytes. Elevated CD4+cell count is one of the pathogenic features for COVID-19 infection.

Creswell et al[23]and Naoroiba et al[24] reported the significant effects of mindfulness meditation training on increasing CD4+ T lymphocyte in HIV patients. The specific T cell responses against SARS CoV 2 are important for the recognition and killing of infected cells, particularly in the lungs of infected individuals. Later, Creswell et al[25] also examine the effect of yoga on transcription level and reported the reduce level of anti- inflammatory transcription factor NK-kappa B which mediate inflammation process and its implication in COVID-19. The authors reported that yoga increased transcription of genes with a GR response element.

Beyond this, one study observed the significant effect of yoga in lowering the cortisol level in breast cancer patients. Cortisol is stress mediators that can down regulate the NF-kB activity and immune function. Reductions in cortisol levels in our study further support the previous studies showed the effect of yoga in improvement in immune functioning. Further, our finding elicit that yoga exert beneficial effect in mucosal immunity. Two studies reported the significant effect of yoga in increasing IgA salivary antibody. IgA is an antibody, commonly found in mucous membranes, mainly in the respiratory and digestive tracts which are the major entry point of SARS-CoV-2 virus. IgA and IgG play important roles in preventing respiratory tract infections.[26] Although no significant effect of yoga were observed in IgG and IgM antibody. Lower immunoglobulin level has been observed in COVID patients. One study[27] observed the significant increase in anti body titre in influenza vaccination while other study reported the significant effect in increase B cell count in breast cancer patients after mediation practice for 6 weeks. In addition, other study observed the effect of yoga on gene expression and found significantly increase anti-influenza antibody compared to control after 4 week and 8 week of follow up. There is no direct study examining the effect of yoga in innate and adaptive immunity of Covid-19 patients. In sum, existing RCT in non- covid clinical and non-clinical individual indicate that practice of yoga and meditation significantly increase the cell counts of both T cells and B cells.

CONCLUSION

The study demonstrated the moderate effect of yoga on immune system through down regulating the pro-inflammatory markers and elevating the cell mediates immunity. It is non-invasive, economic, easy to follow and safe method and underlines its feasibility as complementary therapy for COVID-19 patients. Although, its efficacy as adjuvant is in its infancy. Further extensive studies have been recommended.

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