

# Impact of yoga based mind-body intervention on systemic inflammatory markers and co-morbid depression in active Rheumatoid arthritis patients: A randomized controlled trial.

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### ABSTRACT

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Rheumatoid Arthritis (RA), an autoimmune disorder develops pain, synovitis, cartilage degradation and bony erosion along with showing the symptoms of depression among the patients. Recent studies have shown that mind body interventions like yoga is effective improving quality of life and depression among patients in such autoimmune conditions. This study has shown improvement of systematic inflammatory markers and co-morbid depression among the yoga group of the active RA patients.

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### Introduction

Rheumatoid Arthritis (RA) is an autoimmune disorder having genetic and environmental origin in which joints develop synovitis, cartilage degradation and bony erosion which further leads to deformity and disability. In this condition aging of cells occurs owing to oxidative stress and reduced total anti-oxidation capacity which happens due to inflammation (1). This can cause peroxidation and damage cell membrane and even genetic material. Further, accelerated immune system aging happens and there is immunosenescence which is reduction in immune system response. RA also tends to affect the mental health among patients as evidenced by Matcham et al., owing to 16.8% higher prevalence of depression in patients with RA. (2) Recent studies have shown that Mind Body Interventions (MBI) like yoga is effective improving quality of life and depression among patients in such autoimmune conditions. MBI helps by integrating autoimmune and cognitive behavior of brain associated with emotional, physical change and self-regulation and positive behavioral change (3).

### Study design and results

This was a prospective interventional single site Randomized Controlled Trial (RCT) to analyze effect of eight week Yoga on inflammatory biomarkers and depression among the patients with RA. Patients visiting out-patient department of rheumatology department, were recruited. A total of 108 were assessed for eligibility and 72 participants were recruited and randomized, out of which 60 participants successfully completed the trial.

In Yoga group, a pretested sequence of Asana, pranayama and Dhyana were practiced. This program was conducted five days a week for 120 minute each day. The control group patients followed normal routine along with medications. Primarily severity of the disease was assessed with systemic biomarkers and functional status disease activity. Secondly, changes in severity of depression were analyzed through a questionnaire.

There was a significant increase from baseline levels of Brain-Derived Neurotrophic Factor (BDNF), serotonin,  $\beta$ -endorphins in yoga group as compared to control which play a vital role in neuroplasticity. Systemic inflammatory biomarkers – Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Interleukin-6 (IL-6), Interleukin-17 A (IL-17 A), and Tumor Necrosis Factor-  $\alpha$  (TNF- $\alpha$ ), showed a significant decline which are responsible for aggravating the disease symptoms into patient like pain and inflammation at joints. Anti-inflammatory markers which play a role in immunomodulation, TGF- $\beta$  and soluble Human Leukocyte Antigen – G (HLA-G), showed significant surge. Reactive oxygen species were reduced and increase in total antioxidant capacity, 8OHdG which is a marker of DNA damage was reduced while SIRT1 which is a marker for health span and longevity showed a significant increase. Even telomerase activity showed significant increase in yoga group thus indicating yoga affects cells life span but is also associated with increase in length of telomere length which was not found to have increased in any group.

The secondary outcome of study i.e., depression assessment through Beck's depression inventory-II (BDI-II) showed significant decline in symptoms over eight-week span of intervention as compared to control group.

## Implications

The study showed how yoga based MBI has been beneficial in reducing disease severity and associated symptoms, including benefits on psychological parameters. This helped in improving the life of patients as they were able to do their daily chores with lesser difficulty. This breaks the cycle of stress-autoimmunity exacerbation response. Thus, yoga has been shown to improve mental health of the patient which is negatively associated with the disease severity. Current treatment pivots around joint inflammation but this study shows yoga helps reduce systemic inflammation and stress mediated inflammatory response too. It also helps in maintaining homeostasis of organ system. This is the first study known that has studied HLA-G levels in patients with RA with yoga intervention. HLA-G is known to have anti-inflammatory and immune modulatory effects (4). This study proposes HLA-G can serve as a diagnostic marker and potential treatment target in various autoimmune and inflammatory diseases. This study showed strong association between BDI-II score with disease related disability. Yoga's effect on depression, possibly due to upsurge of neurotransmitters like BDNF, serotonin and  $\beta$ -endorphins which are associated with neuroplasticity (5). The limitation of the study was lack of active control with some physical activity intervention in control group. Also, large scale studies are required for

complete cytokine profile and individual immune effector cell response. But overall study has shown a newer perspective to treat RA with yoga based MBI with strong evidence of molecular mechanism behind its positive effects on physiology and psychology of patient.

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