

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article
ISSN 2394-3211

EJPMR

OPTIMIZE HEALTH THROUGH YOGA & NATUROPATHY - A PREPARATORY MEASURE FOR BETTER IMMUNE RESPONSE DURING COVID-19 PANDEMIC

B. Anasuya* and B. Venkateswar Rao

Central Council for Research in Yoga & Naturopathy, Ministry of AYUSH, New Delhi.

*Corresponding Author: B. Anasuya

Central Council for Research in Yoga & Naturopathy, Ministry of AYUSH, New Delhi.

Article Received on 16/10/2020

Article Revised on 06/11/2020

Article Accepted on 27/11/2020

ABSTRACT

The infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a health crisis having its impact on loss of life, health of the community and economy. There has been a considerable progress in characterizing the virus and development of the vaccine. However, the immediate implementation of the vaccination against COVID-19 may not be possible at present. In current scenario, with relevance to COVID, optimization of health must be the top priority for healthy individuals as well as for individuals with comorbidities. One needs to overcome fear and anxiety and incline towards adopting a healthy lifestyle apart from following the recommended social distancing, quarantine, standard hygiene practices/ guidelines. Yoga and Naturopathy is the traditional and ancient system of medicine that focus on adopting healthy lifestyle and the evidence is extensive that supports positive promotion of health, prevention of diseases, and their role as an adjunct in non-communicable diseases. Though it is too early to comment on the long term complications of COVID, there is a possibility of deconditioning of our body in the phase of post viral infection and yoga and naturopathy may help in restoration of the functional capacity of the system suggesting integration of these therapies for prophylactic, therapeutic and restorative effect which positively influence the clinical course of COVID-19 infection in terms of reduction in severity of signs and symptoms, duration of hospital stay and onset of complications.

KEYWORDS: Yoga; Naturopathy; Immunity; COVID-19; novel coronavirus; health; stress management; cardiorespiratory system.

INTRODUCTION

Recent update of SARS COV 2

The infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a health crisis having its impact on economy, loss of life and overall community health. Public health experts believe that zoonotic viruses are likely to be a continuous threat as virus tends to optimize itself for its current host. Considering the contagiousness of the disease, this new pandemic has become a great concern and challenge to the world. Scientists all over the world are trying to understand the behavior and pathogenesis though not well understood so far. The MERS-CoV and SARS-CoV have been used as the best source of information regarding COVID-19.^[1]

Globally scientists are endeavoring to find effective treatment protocol and were frequently revising the protocols considering their effectiveness in the management of COVID-19. The anti-viral drugs, antimalarial drugs, anti-inflammatory, anti-cytokine therapies and passive immunization using plasma therapy for readily available antibodies are being used according to the clinical manifestations of the disease. Antibodies have become a familiar word in the pandemic

era perhaps giving a hope as the only remedy for combating the corona virus. The interim data of ChAdOx1 nCoV-19 vaccine trials against SARS-CoV-2 indicating of both humoral and cellular immune responses against SARS-CoV-2 from the results that showed a peak on 14th day in spike-specific T-cell responses and by 28th day there was a rise in Anti-spike IgG responses. [2] In addition, detection of SARS-CoV-2reactive CD4+ T cells in unexposed individuals suggested that SARS-CoV-2 and other corona viruses are cross reacting. [3] The long lasting protective response against the virus is still not confirmed by the experts. Though the viruses that cause SARS and COVID-19 are closely related and infect cells the same way, the antibodies produced in response to one type of coronavirus are not cross-protective. However, what would happen in the human body is not known so far potential challenges in the with considerable development of COVID-19 vaccine. [4] Basing on the latest data from COVID-19 vaccine trials, the experts were of the opinion that the detectable T cells which may fight off infection and prevent the COVID-19 disease on re-exposure can offer protection. The other immune system players may still offer longer-lasting immunity. There has been a considerable progress in characterizing

the virus and development of the vaccine which is remarkably robust. However, the immediate implementation of the vaccination against COVID-19 may not be possible at present.

Therefore, in current situation, this health emergency demands strategies that help in the prevention and management of COVID-19 as elderly and individuals with comorbidities like diabetes, hypertension, cardiovascular, respiratory diseases and patients on immunosuppressive therapy are most vulnerable to succumb to this infection. There was also a rise in the number of asymptomatic cases further complicating the transmission and infection rate of this virus. It was reported that 70% of the cases are asymptomatic or very mild that does not require hospitalization while in remaining 30% may suffer from respiratory infection and in severe cases may lead to acute respiratory distress syndrome (ARDS) that requires hospitalization. [5]

From the recent reports of print and social media, the serosurvey in Delhi, a metropolitan city in India has shown antibodies in 23% of the asymptomatic cases with antibody titers ranging from below 10 to 600 or above in individuals recovered from COVID-19. For plasma therapy, plasma with low antibodies was not suitable for transfusion. There are still many unanswered questions like the effectiveness of the vaccine in asymptomatic individuals who already have antibodies especially in individuals with high titers of antibodies against COVID-19. This complex scenario is alerting everyone to focus on optimizing the health for better immune response, prevention of complications and early recovery from corona infection. One needs to overcome fear and adopt healthy lifestyle apart from following recommended social distancing, quarantine and standard hygiene practices/ guidelines. Our focus shifts to enhancing our natural immunity which must be our priority in the current situation. The immune response is known to be dependent on the fitness and immunity level of the person. The clinical presentation of the infection is decided from the interaction between the virulence of the pathogen and immunity of the host. Asymptomatic cases of novel coronavirus is partially indicating the dominance of host immunity and there is no enough evidence on the virulence of the pathogen so far.

Ancient system of medicine in India

Yoga and Naturopathy is a traditional and ancient system of medicine and one of the AYUSH systems of medicine. They focus on adopting a disciplined healthy lifestyle like regular meal and sleep timings, preference to healthy food choices, regular yoga for physical fitness and psychological stress reduction, and fasting at regular intervals for detoxification which either directly or indirectly promote health and vitality. The evidence is extensive for Yoga and Naturopathy that supports the positive promotion of health, prevention of diseases, and their role as an adjunct in noncommunicable diseases in optimizing the baseline

immunity level. Proper hydration, intake of a healthy balanced diet rich in vitamins, minerals, proteins, including foods rich in zinc and selenium for their antioxidant properties are also recommended.

The genetic variability in the human race is the focal point for human responses to a variety of stimulus and the human body is equipped with a sophisticated response mechanism for the maintenance of optimal health. They focus on the origins of health rather than the pathogenesis of the disease. The factors that promote health and increase vitality are inversely associated to the onset of diseases and also the pathogenesis of the The pandemic era of COVID-19 has strengthened our thought process on salutogenesis and to acquire a state of wellbeing at all levels resulting in Eudaimonic wellbeing. In the process of adapting to new normal circumstances stress, anxiety, and depression are becoming a cause of worry. While non-pharmacological methods of stress reduction have been in practice since long time among several cultures, only in the recent past such practices are gaining acceptance worldwide. Translating information on stress reduction from ancient cultures into modern scientific literature is important to preserve and propagate such wellness practices in the management of various illnesses.

Scientific basis of Yoga and Naturopathy

The practice of asanas, pranayama and meditation can impact wellness, immune function, and longevity. Recent evidence has reported higher viral loads of SARS-CoV-2 in nose than throat and was similar in both symptomatic and asymptomatic cases. [8] Post-hoc secondary analysis of data from viral intervention study on upper respiratory tract infection due to SARS COV 2 has shown a reduction of duration by an average of two-and-a-half days with nasal irrigation also known as Jalaneti in yoga along with gargling with warm saline water, [9] possibly their role in shedding the virus. In older adults, yoga poses like dog pose, triangular pose and warrior pose have shown to increase the expression of human β defensing 2.[10] This will increase the mucosal immunity and is also negatively associated to cortisol levels. The practice of transcendental meditation was observed to have higher CD3+CD4-CD8+ lymphocytes and natural killer cells compared to controls which explains the significant effect on neuroendocrine axis and its association with the immune system.^[11] Stress not only influence the pathogenesis of the diseases but also affects the cellular aging in healthy individuals. Recent studies indicate that yoga could play a key role in combating stress, anxiety, and depression. Yoga-based lifestyle was shown to decreases the expression of pro-inflammatory genes and increases the expression of anti-inflammatory genes and may also play an important immunemodulatory role in a cytokine storm. The beneficial role of components of yoga as an adjunct was reported in diseases like pulmonary tuberculosis, [12] influenza [13] and HIV. [14,15] The classic components of Yoga that includes asanas (physical postures), pranayama (breathing

exercises), and dhyana (Meditation) which are derived from a mix of Hatha Yoga and Raja Yoga have shown a significant improvement in the cardinal biomarkers of cellular aging and the metabotropic biomarkers influencing cellular aging compared to baseline values after 12 weeks of intervention in healthy individuals. The mean levels of DNA damage marker 8-OH2dG, oxidative stress markers reactive oxygen species, metabotropic blood biomarkers that include cortisol and IL-6 were significantly lower while mean levels of TAC. telomerase activity, β-endorphin, BDNF and sirtuin-1 have significantly increased post-intervention. Though the increase in the mean level of telomere length was not significant, yogic intervention has shown to help in reducing the rate of cellular aging in an apparently healthy population. [16] In addition, a decrease in severity in the major depressive disease was evident from significant decrease in BDI-II score and a significant increase in telomerase activity levels, BDNF (ng/ml), DHEAS, sirtuin 1 and decrease in IL-6 and cortisol levels. These findings suggested a decrease in severity in major depressive disease with short term yoga- and meditation-based lifestyle intervention association with an increase in neuroplasticity, by significantly improving brain physiology, mind-body communication (MBC), and cellular health. Moreover, practice of yoga was reported to reduce relapses. Therefore yoga module can be used as an ideal therapeutic intervention in major depressive disease management. [17] Yoga therapy also known as mind body medicine was proposed to communicate between body and mind through an integration of top-down and bottom-up processes. Topdown processes reduces psychological stress by the down regulation of the hypothalamic-pituitary axis (HPA) and sympathetic nervous system (SNS) activity via SAM axis resulting in modulation of immune response and inflammation. Similarly, volitional breathing maneuvers like pranayama and asanas that influences the musculoskeletal, cardiovascular and nervous system function is influenced by bottom up processes which in turn modulate the immune function and emotional wellbeing via reactivation of the parasympathetic activity and also by reducing the predominance of sympathetic activity. [18] The enhanced production of pro-inflammatory cytokines and higher oxygen consumption was shown to be associated with higher sympathetic tone, [19] while studies on meditation have shown to be negatively associated with pro inflammatory cytokines. The practice of yoga and meditation was shown to have positive effects in reducing inflammation. [20] The changes in natural killer activity observed during practice of pranayama was positively correlated to alpha rhythms. [21]

In HIV patients, a decrease in viral load and increase in CD 4 cells was also reported indicating the yoga as an immune boosting module even in immunosuppressive conditions. Yoga optimizes the immune function through activation of both pro inflammatory and anti-inflammatory cytokines in a precise balanced manner

either to promote inflammation of suppress infection according to the body's requirement. [23] The practice of transcendental meditation increases B lymphocyte series with concomitant increase in natural killer cells. [24] The expression levels of interferon $\gamma(IFN-\gamma)$ increased while the expression levels of TNF-α and IL-6 reduced with mindfulness meditation suggesting restoration of immune function in women diagnosed with breast cancer, [25] and also in primary open-angle glaucoma patients. [26] The C reactive protein in overweight or overstressed adults presented with high inflammation was also reported to be reduced in people with mindfulness meditation. [27] The mechanism behind the treatment of major depressive disorder inflammation-related diseases have shown downregulation of the expression of the proinflammatory gene COX2 which is linked to the deacetylated HDAC activity. [28] The role of meditation as an anti-aging strategy, [29] is highlighted possibly due to the involvement of various genomic regions related with cardiovascular diseases, neurological and mental illnesses, and cancer as well.

Naturopathy is a science of healthy living with the adoption of disciplined life style. The different modalities used are therapeutic fasting, diet therapy, heliotherapy, mud therapy hydrotherapy, massage therapy etc. The somatotropin hormone (STH) activity is increased with whole-body hyperthermic bath under hydrotherapy in addition to higher relative counts of CD8+ lymphocytes and NK cells. [31] Fasting therapy is one of the important components of naturopathy used for detoxification of the body. [30] Overconsumption coupled with a sedentary life is one of the leading causes of metabolic morbidity. Fasting therapy has benefits that include decreased blood glucose levels growth factor signaling and the activation of stress resistance pathways that affect cell growth, metabolism, and protection against inflammation, oxidative stress, and even cell death.^[32] In modern terminology, fasting, also known as a time-restricted feeding model was shown to reset the phase of hepatic circadian rhythm possibly by optimizing the metabolic regulators of glucose and fatty acids metabolism.^[33] Intermittent fasting with water for 20 hrs every second day for 15 days has shown a consistently increased insulin sensitivity with significant increased insulin-mediated whole-body glucose uptake rate in healthy individuals, [34] and was shown to improve oxidative stress with increased glutathione and reduced serum malondialdehyde levels. These findings were also observed to be maintained for six weeks even after stopping fasting in hypertensives, [35] and diabetic subjects. [36] Fasting also reduces interleukin 6, C-reactive protein and homocysteine levels.^[37] In physiological conditions, the damaged cells will be replaced with new cells by a process of autophagy. [38] The upregulation of autophagy happens in response to nutrient deprivation also. [39,40] Calorie or nutrient restriction has also been a promising strategy to modulate autophagy and enhance the efficacy of anticancer therapies while protecting normal cells. The development of age-related diseases such as diabetes, cancer, and neurodegenerative and cardiovascular diseases were also reported to be reduced. [41]

Another important component for optimum vitality is regular sleep timings as proposed by Yoga and Naturopathy. The interaction of sleep wake cycle with immune function is complex. As modern population study on the influence of sleep on immunological memory cells response has shown markedly increased Ag-specific IgG1 after vaccinated against hepatitis indicating boosting of immunological memory with sleep. There was a remarkable decrease in TNF-alpha producing CD8+ cells. Sleep with its association with high growth hormone and low catecholamine and cortisol levels also has a specific role in proinflammatory endocrine set up resulting in improving the immunological memory. [42–44] Therefore, acute sleep deprivation is associated with lower production of antigen-specific antibodies in the very early stage of an adaptive immune response to influenza vaccination. [45] In real time, prolonged sleep deprivation observed in the modern population has become common on a daily basis. While in the management of COVID-19, qualitative sleep is believed to play a significant role in the modulation of the immune response to combat this novel virus. The apparently simple principles for healthy living has a hidden treasure of beautiful health, a life just beyond survival. A state of wellbeing at all levels. In the present scenario, extreme age groups and individuals with comorbidities are at higher risk of infection and mortality with complications of novel coronavirus.

CONCLUSION

Earlier, Yoga and Naturopathy is predominantly categorized as preventive medicine. But, later, due to their effectiveness on the stress coping abilities, modulation of neuroendocrine, autonomic and immune system in healthy, elderly and also in non-communicable diseases have led to wider acceptance of yoga and naturopathy in the health care system. Though, their efficacy has never been tested in acute phases of diseases, Yoga and Naturopathic principles very much advised to be follow in non-acute phases for positive promotion of health and prevent or delay the onset of complications. In current scenario, with relevance to COVID-19, optimization of health must be the top priority for healthy individuals as well as for individuals with comorbidities. The evidence clearly indicates that the health promoting principles of yoga & naturopathy helps in modulation of the inflammatory and immune responses which may influence the clinical manifestation of the COVID-19. Though long term complications of COVID-19 has not been confirmed, there is a possibility of deconditioning of our body in the phase of post viral infection. Hence, positively yoga and naturopathy may also help in the restoration of health by regaining the functional capacity of our system.

Conflict of Interest: None.

REFERENCES

- 1. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. *J Pharm Anal*, 2020; 10(2):102-108. doi:10.1016/j.jpha.2020.03.001.
- 2. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet*, 2020; 0(0): 1-13. doi:10.1016/S0140-6736(20)31604-4.
- 3. Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. *Cell*, 2020; 181(7): 1489-1501. e15. doi:10.1016/j.cell.2020.05.015
- 4. Lv H, Wu NC, Mok CKP. COVID-19 vaccines: Knowing the unknown. *Eur J Immunol*, 2020; 50(7): 939-943. doi:10.1002/eji.202048663
- Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19). StatPearls Publishing, 2020.
 - http://www.ncbi.nlm.nih.gov/pubmed/32150360. Accessed July 31, 2020.
- Yoga | Ministry of AYUSH | GOI https://main.ayush.gov.in/about-the-systems/yoga. Accessed July 31, 2020.
- Naturopathy | Ministry of AYUSH | GOI. https://main.ayush.gov.in/about-thesystems/naturopathy. Accessed July 31, 2020.
- 8. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med*, 2020; 382(12): 1177-1179. doi:10.1056/NEJMc2001737.
- 9. Ramalingam S, Graham C, Dove J, Morrice L, Sheikh A. Hypertonic saline nasal irrigation and gargling should be considered as a treatment option for COVID-19. *J Glob Health*, 2020; 10(1): 10332. doi:10.7189/JOGH.10.010332
- 10. Eda N, Shimizu K, Suzuki S, Tanabe Y, Lee E, Akama T. Effects of yoga exercise on salivary beta-defensin 2. *Eur J Appl Physiol*, 2013; 113(10): 2621-2627. doi:10.1007/s00421-013-2703-y.
- 11. Infante J, Peran F, Rayo J, et al. Levels of immune cells in transcendental meditation practitioners. *Int J Yoga*, 2014; 7(2): 147. doi:10.4103/0973-6131.133899.
- 12. Visweswaraiah NK, Telles S. Randomized trial of yoga as a complementary therapy for pulmonary tuberculosis. *Respirology*, 2004; 9(1): 96-101. doi:10.1111/j.1440-1843.2003.00528.x
- 13. Obasi CN, Brown R, Ewers T, et al. Advantage of meditation over exercise in reducing cold and flu illness is related to improved function and quality of life. *Influenza Other Respi Viruses*, 2013; 7(6): 938-944. doi:10.1111/irv.12053.
- 14. Naoroibam R, Metri K, Bhargav H, Nagaratna R,

- Nagendra H. Effect of Integrated Yoga (IY) on psychological states and CD4 counts of HIV-1 infected Patients: A Randomized controlled pilot study. *Int J Yoga*, 2016; 9(1): 57. doi:10.4103/0973-6131.171723.
- 15. Dunne EM, Balletto BL, Donahue ML, et al. The benefits of yoga for people living with HIV/AIDS: A systematic review and meta-analysis. *Complement Ther Clin Pract*, 2019; 34: 157-164. doi:10.1016/j.ctcp.2018.11.009
- Tolahunase M, Sagar R, Cellular RD-O medicine and, 2017 U. Impact of yoga and meditation on cellular aging in apparently healthy individuals: a prospective, open-label single-arm exploratory study. *Oxid Med Cell Longev*, 2017; 2017(2784153.). https://www.hindawi.com/journals/omcl/2017/79289 81/abs/. Accessed July 30, 2020.
- 17. Tolahunase MR, Sagar R, Faiq M, Dada R. Yogaand meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive disorder: A randomized controlled trial. *Restor Neurol Neurosci*, 2018; 36(3): 423-442. doi:10.3233/RNN-170810.
- 18. Taylor AG, Goehler LE, Galper DI, Innes KE, Bourguignon C. Top-Down and Bottom-Up Mechanisms in Mind-Body Medicine: Development of an Integrative Framework for Psychophysiological Research. *Explor J Sci Heal*, 2010; 6(1): 29-41. doi:10.1016/j.explore.2009.10.004.
- 19. Tracey KJ. The inflammatory reflex. *Nature*, 2002; 420(6917): 853-859. doi:10.1038/nature01321.
- 20. Kiecolt-Glaser JK, Christian L, Preston H, et al. Stress, inflammation, and yoga practice. *Psychosom Med*, 2010; 72(2): 113-121. doi:10.1097/PSY.0b013e3181cb9377.
- 21. Kamei T, Toriumi Y, Kimura H, Kimura K. Correlation between alpha rhythms and natural killer cell activity during yogic respiratory exercise. *Stress Heal*, 2001; 17(3): 141-145. doi:10.1002/smi.889.
- 22. Naoroibam R, Metri K, Bhargav H, Nagaratna R, Nagendra H. Effect of Integrated Yoga (IY) on psychological states and CD4 counts of HIV-1 infected Patients: A Randomized controlled pilot study. *Int J Yoga*, 2016; 9(1): 57. doi:10.4103/0973-6131.171723.
- 23. Cahn BR, Goodman MS, Peterson CT, Maturi R, Mills PJ. Yoga, meditation and mind-body health: Increased BDNF, cortisol awakening response, and altered inflammatory marker expression after a 3-month yoga and meditation retreat. Front Hum Neurosci, 2017; 11(315). doi:10.3389/fnhum.2017.00315
- 24. Xiang YT, Yang Y, Li W, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The Lancet Psychiatry*, 2020; 7(3): 228-229. doi:10.1016/S2215-0366(20)30046-8
- 25. Witek Janusek L, Tell D, Mathews HL. Mindfulness based stress reduction provides psychological

- benefit and restores immune function of women newly diagnosed with breast cancer: A randomized trial with active control. *Brain Behav Immun*, 2019; 80: 358-373. doi:10.1016/j.bbi.2019.04.012.
- 26. Dada T, Mittal D, Mohanty K, et al. Mindfulness meditation reduces intraocular pressure, lowers stress biomarkers and modulates gene expression in Glaucoma: A randomized controlled trial. *J Glaucoma*, 2018; 27(12): 1061-1067. doi:10.1097/IJG.0000000000001088.
- 27. Villalba DK, Lindsay EK, Marsland AL, et al. Mindfulness training and systemic low-grade inflammation in stressed community adults: Evidence from two randomized controlled trials. *PLoS One*, 2019; 14(7). doi:10.1371/journal.pone.0219120.
- 28. Chaix R, Alvarez-López MJ, Fagny M, et al. Epigenetic clock analysis in long-term meditators. *Psychoneuroendocrinology*, 2017; 85: 210-214. doi:10.1016/j.psyneuen.2017.08.016.
- García-Campayo J, Puebla-Guedea M, Labarga A, et al. Epigenetic Response to Mindfulness in Peripheral Blood Leukocytes Involves Genes Linked to Common Human Diseases. *Mindfulness (N Y)*, 2018; 9(4): 1146-1159. doi:10.1007/s12671-017-0851-6.
- 30. Rastogi R, Rastogi D. Fasting as a curative practice: Historical, traditional, and contemporary perspective. In: *Ayurvedic Science of Food and Nutrition*. Vol 9781461496281. Springer New York, 2014; 123-135. doi:10.1007/978-1-4614-9628-1 10.
- 31. Blazícková S, Rovenský J, Koska J, Vigas M. Effect of hyperthermic water bath on parameters of cellular immunity. *Int J Clin Pharmacol Res*, 2000; 20(1-2): 41-46.
 - http://www.ncbi.nlm.nih.gov/pubmed/11146901. Accessed August 2, 2020.
- 32. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev.*, 2017; 39: 46-58. doi:10.1016/j.arr.2016.10.005.
- 33. Satoh Y, Kawai H, Kudo N, Kawashima Y, Mitsumoto A. Time-restricted feeding entrains daily rhythms of energy metabolism in mice. *Am J Physiol Integr Comp Physiol*, 2006; 290(5): R1276-R1283. doi:10.1152/ajpregu.00775.2005.
- 34. Halberg N, Henriksen M, Söderhamn N, et al. Effect of intermittent fasting and refeeding on insulin action in healthy men. *J Appl Physiol*, 2005; 99(6): 2128-2136. doi:10.1152/japplphysiol.00683.2005.
- 35. Al-Shafei AIM. Ramadan fasting ameliorates arterial pulse pressure and lipid profile, and alleviates oxidative stress in hypertensive patients. *Blood Press*, 2014; 23(3): 160-167. doi:10.3109/08037051.2013.836808
- 36. Al-Shafei AI. Ramadan fasting ameliorates oxidative stress and improves glycemic control and lipid profile in diabetic patients. *Eur J Nutr*, 2014; 53(7): 1475-1481. doi:10.1007/s00394-014-0650-y.
- 37. Faris MAIE, Kacimi S, Al-Kurd RA, et al.

- Intermittent fasting during Ramadan attenuates proinflammatory cytokines and immune cells in healthy subjects. *Nutr Res*, 2012; 32(12): 947-955. doi:10.1016/j.nutres.2012.06.021
- 38. Glick D, Barth S, Macleod KF. Autophagy: Cellular and molecular mechanisms. *J Pathol*, 2010; 221(1): 3-12. doi:10.1002/path.2697.
- 39. Shang L, Chen S, Du F, Li S, Zhao L, Wang X. Nutrient starvation elicits an acute autophagic response mediated by Ulk1 dephosphorylation and its subsequent dissociation from AMPK. *Proc Natl Acad Sci U S A.*, 2011; 108(12): 4788-4793. doi:10.1073/pnas.1100844108.
- 40. Kroemer G, Mariño G, Levine B. Autophagy and the Integrated Stress Response. *Mol Cell*, 2010; 40(2): 280-293. doi:10.1016/j.molcel.2010.09.023.
- 41. O'Flanagan CH, Smith LA, McDonell SB, Hursting SD. When less may be more: Calorie restriction and response to cancer therapy. *BMC Med*, 2017; 15(1): 106. doi:10.1186/s12916-017-0873-x.
- 42. Lange T, Dimitrov S, Bollinger T, Diekelmann S, Born J. Sleep after Vaccination Boosts Immunological Memory. *J Immunol*, 2011; 187(1): 283-290. doi:10.4049/jimmunol.1100015.
- 43. Besedovsky L, Lange T, Born J. Sleep and immune function. *Pflugers Arch Eur J Physiol*, 2012; 463(1): 121-137. doi:10.1007/s00424-011-1044-0.
- 44. Dimitrov S, Lange T, Tieken S, Fehm HL, Born J. Sleep associated regulation of T helper 1/T helper 2 cytokine balance in humans. *Brain Behav Immun*, 2004; 18(4): 341-348. doi:10.1016/j.bbi.2003.08.004.
- 45. Benedict C, Brytting M, Markström A, Broman JE, Schiöth HB. Acute sleep deprivation has no lasting effects on the human antibody titer response following a novel influenza A H1N1 virus vaccination. *BMC Immunol*, 2012; 13(1): 1. doi:10.1186/1471-2172-13-1.

www.ejpmr.com Vol 7, Issue 12, 2020. ISO 9001:2015 Certified Journal 492