



## Original Research Article

# EFFECT OF YOGA ON CALCITONIN GENE- RELATED PEPTIDE(CGRP) AND LH/HF RATIO PARAMETER OF HEART RATE VARIABILITY(HRV) IN MIGRAINE PATIENTS

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### ABSTRACT

**Background:** Migraine involves neurovascular and autonomic dysfunction. Yoga may decrease CGRP levels and improve heart rate variability balance. The aim is to determine the Effect of yoga on Calcitonin Gene Related Peptide (CGRP) And LH/HF Ratio parameter of Heart Rate Variability (HRV) in migraine patients.

**Materials and Methods:** This analytical observational study included 80 migraine patients divided into two groups two groups A. Yoga conventional care group B. conventional care group without Yoga at RMLIMS, Lucknow. Patients aged 18–50 years meeting ICHD-3 criteria were included. CGRP was measured by ELISA, and LF/HF ratio was assessed using software LABCHART PRO v8.1.8 with HRV module v2.0.3. Written informed consent was obtained from all participants.

**Results:** Serum CGRP levels decreased significantly over 12 weeks in both groups, with a greater reduction observed in the yoga group. Baseline CGRP levels showed no significant difference between non-yoga and yoga groups. After 12 weeks, CGRP reduction was statistically significant higher in the yoga group, indicating enhanced improvement with yoga intervention. Intragroup analysis showed highly significant reductions in both groups, but the magnitude was greater with yoga practice.

LF/HF ratio showed no baseline difference between groups. After 12 weeks, the yoga group demonstrated a statistically significant reduction in LF/HF ratio, while the non-yoga group showed no significant change, indicating improved autonomic balance associated with yoga practice.

**Conclusion:** Yoga statistically significant reduces CGRP levels and improves autonomic balance in migraine patients, supporting its role as a safe, effective adjunct therapy targeting neurochemical and autonomic mechanisms.

**Keywords:** Migraine, Yoga therapy, Calcitonin Gene-Related Peptide (CGRP), Heart Rate Variability (HRV), LF/HF ratio.

## INTRODUCTION

Migraine is a common and disabling neurovascular disorder characterized by recurrent headache episodes associated with sensory, autonomic, and cognitive symptoms. It affects a significant proportion of the global population and contributes

substantially to reduced quality of life and work productivity. Increasing evidence suggests that migraine is not only a pain disorder but also involves complex neurovascular, inflammatory, and autonomic mechanisms. Understanding these mechanisms is essential for developing integrative therapeutic approaches that are safe, cost-effective, and suitable for long-term management.<sup>[1]</sup>

Calcitonin gene-related peptide (CGRP) has emerged as a key neuropeptide in migraine pathophysiology. It is released from trigeminal nerve terminals during migraine attacks and contributes to vasodilation, neurogenic inflammation, and pain transmission within the trigeminovascular system. Elevated CGRP levels during attacks and the ability of exogenous CGRP to trigger migraine-like symptoms strongly support its central role in disease mechanisms and therapeutic targeting.<sup>[2]</sup>

Autonomic nervous system dysfunction is another important component of migraine. Heart rate variability (HRV), particularly the low-frequency to high-frequency (LF/HF) ratio, reflects sympathovagal balance. Studies indicate altered HRV parameters in migraine patients, suggesting increased sympathetic dominance and reduced parasympathetic activity, which may contribute to attack susceptibility and disease chronicity.<sup>[3]</sup>

Yoga, a mind-body intervention combining physical postures, breathing techniques, and meditation, has shown potential in modulating neuroendocrine and autonomic pathways. Evidence suggests yoga practice improves HRV indices and may reduce migraine frequency and severity through stress reduction, autonomic balance restoration, and neurochemical modulation. However, limited studies have explored its effect on CGRP levels alongside HRV parameters in migraine patients.<sup>[4]</sup> Therefore, evaluating the effect of yoga on CGRP levels and LF/HF ratio of HRV may provide valuable insights into non-pharmacological mechanisms of migraine management and support integrative therapeutic strategies.

## MATERIALS AND METHODS

This was an Analytical Observational study was carried out on 80 migraine patients and there was two groups A. Yoga conventional care group B. conventional care group without Yoga in Department of Physiology, RMLIMS, Lucknow. Ethical clearance was obtained from the RMLIMS Institutional Ethics Committee (IEC No. 79/24). Migraine patients of aged between 18 years to 50 years of both the genders, were recruited from the Neurology OPD of Dr. RMLIMS, Lucknow. The inclusion criteria was Diagnosed case of migraine patients fulfilling diagnostic criteria of ICH 3rd

edition (beta version) of headache, Age group from 18 to 50 years, Giving consent for study and willing for yoga as per protocol. Patients excluded were those have Diabetes, Hypertension, Hyperlipidemia, Pregnancy or Lactation, Allergy or Inflammation, Regular use of vasoactive drugs, Any comorbidity interfering with yogic exercise.

Written informed consent is taken from all the subjects. Estimation of Serum level CGRP was measured in the laboratory, in Department of Biochemistry, Dr. RMLIMS, Lucknow. CGRP was done by ELISA method and measurement of LF/HF Ratio was done by the computer and the software LABCHART PRO v8.1.8 with HRV module v2.0.3 was turned on in Physiology Department, Dr. RMLIMS, Lucknow.

At the end of study using MS excel and R-4.2.3 statistical software for data entry and data analysis. Here under consideration of study variable measured as continuous and categorical formal. Continuous variable presented as Mean  $\pm$  SD and categorical variable presented in frequency and percentage. For normality testing using Shapiro-Wilk test. After that apply parametric tests otherwise non-parametric test. Parametric tests, including the Student's paired t-test and unpaired t-test, were used as appropriate. Non-parametric tests, including the Wilcoxon signed-rank test, Mann-Whitney U test, and Kruskal-Wallis test, were applied where appropriate. A p-value of  $<0.05$  was considered statistically significant.

## RESULTS

The CGRP levels (pg/mL) showed notable changes between the groups and over time. At baseline, the mean CGRP level was  $239.66 \pm 129.15$  pg/mL in migraine patients without yoga and  $209.75 \pm 127.12$  pg/mL in those with yoga, with no significant difference between the groups ( $t = -1.04$ ,  $p = 0.300$ ). After 12 weeks, CGRP levels decreased to  $218.91 \pm 125.72$  pg/mL in the non-yoga group and more markedly to  $147.16 \pm 122.85$  pg/mL in the yoga group, showing a significant between-group difference ( $t = -2.58$ ,  $p = 0.012$ ). Intragroup analysis revealed highly significant reductions in CGRP levels within both groups over time ( $t = 8.17$ ,  $p < 0.001$  for the non-yoga group and  $t = 8.86$ ,  $p < 0.001$  for the yoga group), indicating greater improvement in patients practicing yoga.

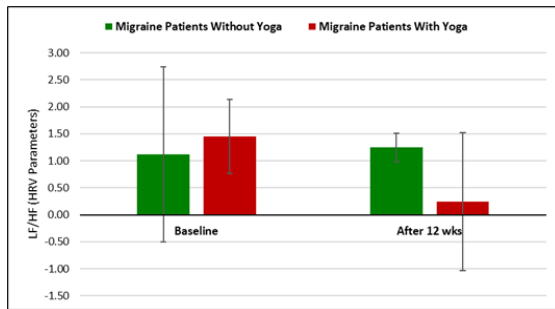
**Table 1: Intergroup & Intragroup Comparison of CGRP**

CGRP (pg/mL)	Migraine Patients Without Yoga	Migraine Patients With Yoga	unpaired t test	
	Mean $\pm$ SD	Mean $\pm$ SD	t-value	p-value
Baseline	239.66 $\pm$ 129.15	209.75 $\pm$ 127.12	-1.04	0.300
After 12 wks	218.91 $\pm$ 125.72	147.16 $\pm$ 122.85	-2.58	0.012
Intragroup	t=8.17, p<0.001		t=8.86, p<0.001	

The LF/HF ratio (HRV parameter) in migraine patients showed notable changes over 12 weeks, particularly in those practicing yoga. At baseline,

the LF/HF ratio was  $1.12 \pm 0.68$  in the non-yoga group and  $1.45 \pm 1.62$  in the yoga group, with no significant difference between groups ( $t = 1.18$ ,  $p =$

0.240). After 12 weeks, the ratio was  $1.25 \pm 1.28$  in the non-yoga group and markedly lower at  $0.24 \pm 0.26$  in the yoga group, demonstrating a significant between-group difference ( $t = -4.86, p < 0.001$ ). Intragroup analysis revealed no significant change in the non-yoga group over time ( $t = 0.70, p = 0.489$ ), whereas the yoga group experienced a significant reduction in LF/HF ratio ( $t = 5.05, p < 0.001$ ), indicating improved autonomic balance with yoga intervention.



**Figure 1: Intergroup & Intragroup Comparison of HRV Parameter – LF/HF Ratio.**

## DISCUSSION

The present study demonstrates that yoga intervention in migraine patients results in significant reductions in serum CGRP levels along with improvement in autonomic balance, as reflected by reduction in the LF/HF ratio of heart rate variability (HRV). These findings support the current understanding that migraine is a complex neurovascular disorder involving neurochemical and autonomic dysregulation, both of which may be modified by integrative non-pharmacological therapies such as yoga.<sup>[2,5]</sup> Similar observations have been reported by Kisan et al., who demonstrated improvement in autonomic function and clinical outcomes in migraine patients following yoga intervention.<sup>[1]</sup>

CGRP is a key neuropeptide involved in migraine pathophysiology and plays a major role in trigeminovascular activation, neurogenic inflammation, and vasodilation.<sup>[2]</sup> Elevated CGRP levels have been consistently reported in migraine patients, and reduction in CGRP is associated with clinical improvement.<sup>[7]</sup> The findings of the present study, showing significant reduction in CGRP levels particularly in the yoga group, are in agreement with previous studies. Schytz et al. and Tuka et al. also reported increased CGRP levels in migraine patients and reduction following effective treatment.<sup>[9,8]</sup> These similarities suggest that yoga may influence neuropeptide modulation through neuroendocrine and stress-related pathways.

The mechanism by which yoga reduces CGRP levels is likely multifactorial. Yoga is known to reduce sympathetic overactivity, regulate hypothalamic-pituitary-adrenal axis function, and reduce stress hormone levels. Similar findings were

reported by Streeter et al., who suggested that yoga influences autonomic and neuroendocrine regulation through GABAergic and parasympathetic pathways.<sup>[13]</sup> Additionally, Goadsby et al. highlighted the interaction between stress pathways and trigeminovascular activation in migraine pathogenesis.<sup>[5]</sup>

Autonomic dysfunction is another important feature of migraine. HRV analysis is a well-established non-invasive tool for evaluating sympathovagal balance. Migraine patients often demonstrate increased sympathetic activity and reduced parasympathetic activity. Kim et al. reported reduced HRV and altered autonomic balance in migraine patients compared to controls.<sup>[3]</sup> The present study showed no significant baseline difference between groups, confirming comparability. However, after 12 weeks, a significant reduction in LF/HF ratio was observed in the yoga group, indicating improved autonomic balance.

These findings are consistent with previous yoga-based HRV studies. Tyagi et al. demonstrated improvement in parasympathetic activity and HRV parameters following yoga interventions.<sup>[10]</sup> Similarly, Giridharan et al. reported significant improvement in HRV indices following yoga-based interventions.<sup>[4]</sup> Lehrer et al. also demonstrated improvement in autonomic regulation through breathing-based therapies and HRV modulation techniques.<sup>[11]</sup>

Breathing techniques used in yoga may contribute significantly to autonomic regulation. Bernardi et al. demonstrated that slow breathing improves baroreflex sensitivity and enhances vagal activity.<sup>[12]</sup> These physiological mechanisms may explain the significant reduction in LF/HF ratio observed in the yoga group in the present study.

Similar improvements in autonomic balance following yoga have been observed in other chronic disease populations. Cramer et al. demonstrated beneficial effects of yoga in chronic pain conditions through autonomic modulation and stress reduction.<sup>[14]</sup> Wells et al. also reported improvement in migraine frequency and severity with mind-body therapies including yoga.<sup>[15]</sup> These findings support the broader therapeutic potential of yoga beyond symptomatic relief.

The combined reduction in CGRP levels and LF/HF ratio observed in this study suggests an interaction between neurochemical and autonomic pathways in migraine. Goadsby et al. emphasized the role of central sensitization, neuropeptide release, and autonomic dysregulation in migraine pathophysiology.<sup>[5]</sup> The present findings support the hypothesis that yoga may act through integrated neurochemical and autonomic modulation.

From a clinical perspective, these findings support the use of yoga as an adjunct therapy in migraine management. Pharmacological therapies targeting CGRP pathways are effective but may be expensive and associated with long-term safety

considerations.<sup>[7]</sup> In contrast, yoga is safe, cost-effective, and suitable for long-term practice, particularly in resource-limited settings.

The present study has several strengths. It simultaneously evaluates biochemical and physiological parameters, providing a comprehensive understanding of migraine modulation. The longitudinal design allows assessment of temporal changes, and inclusion of a control group improves internal validity.

However, some limitations should be acknowledged. The sample size may limit generalizability. Variability in CGRP assay techniques across studies may limit direct comparison. Additionally, confounding factors such as lifestyle patterns, stress levels, and medication use may influence HRV and CGRP levels. Future studies should include larger sample sizes, multicenter designs, and longer follow-up duration. Further research should also evaluate correlations between CGRP reduction, HRV improvement, and clinical outcomes such as headache frequency and disability scores.

Future studies should also explore dose-response relationships between yoga duration and physiological outcomes. Incorporation of neuroimaging techniques and inflammatory biomarker analysis may provide deeper insight into mechanisms underlying yoga-induced migraine improvement.

In conclusion, the present study demonstrates that yoga significantly reduces CGRP levels and improves autonomic balance in migraine patients. These findings support integration of yoga into comprehensive migraine management strategies and highlight its role in modulating both neurochemical and autonomic pathways involved in migraine pathophysiology.

**Novelty:** No any previous study was conducted based on the effect of yoga on CGRP levels in migraine patients.

**Limitations:** The present study was conducted with a relatively small sample size, which may limit the statistical power of the findings and restrict the generalizability of the results to the broader migraine population. The absence of a true control group limits the ability to attribute observed changes exclusively to the yoga intervention, as external factors cannot be completely ruled out. The short duration of the yoga intervention may not have been sufficient to capture long-term or sustained effects on autonomic function, biomarkers, headache burden, and quality of life.

## CONCLUSION

The present study demonstrates that yoga intervention significantly reduces serum CGRP levels and improves autonomic balance, as reflected by a reduction in LF/HF ratio of HRV, in patients with migraine. These findings suggest that yoga may modulate both neurochemical and autonomic pathways involved in migraine pathophysiology. The greater improvement observed in the yoga group highlights its potential role as an effective adjunctive therapy in migraine management. Considering its safety, cost-effectiveness, and feasibility for long-term practice, yoga may be integrated into comprehensive migraine treatment strategies. Further large-scale studies are recommended to confirm these findings and explore long-term clinical benefits and underlying mechanisms.

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