RESEARCH PAPER

"Association Between Anxiety Severity and Cardiovascular Autonomic Functions in Newly Diagnosed, Untreated Patients with Essential Hypertension: A Cross-Sectional Analytical Study"

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ABSTRACT

Background: Anxiety may influence cardiovascular autonomic regulation through interactions between central emotional-processing pathways and the autonomic nervous system. However, the relationship between anxiety severity and individual cardiovascular autonomic function parameters in newly diagnosed, untreated patients with essential hypertension require further investigation.

Aim: To evaluate the association between anxiety severity and cardiovascular autonomic function in newly diagnosed, untreated patients with essential hypertension.

Materials and Methods: This cross-sectional analytical study included 50 newly diagnosed, untreated patients with essential hypertension aged 36–55 years. Anxiety severity was assessed using the Hamilton Anxiety Rating Scale (HAMA). Cardiovascular autonomic function was evaluated using six tests: the 30:15 ratio, Deep Breathing Test (DBT), Valsalva manoeuvre, Lying-to-Standing Test (LST), Hand Grip Test (HGT) and Cold Pressor Test (CPT). Correlation analysis was used to examine associations between HAMA scores and autonomic function parameters. Multiple linear regression was performed to assess the association between HAMA score and Valsalva ratio after adjustment for age, sex, body mass index (BMI) and waist-to-hip ratio (WHR).

Results: The mean age of the participants was 41.26 ± 4.43 years, mean BMI was 27.15 ± 3.29 kg/m², mean systolic blood pressure was 167.76 ± 14.11 mmHg, mean diastolic blood pressure was 99.20 ± 7.99 mmHg, and mean HAMA score was 9.38 ± 2.81. HAMA score showed a significant moderate negative correlation with Valsalva ratio (r=-0.415, p=0.003). No statistically significant correlations were observed with the 30:15 ratio, DBT, LST, HGT and CPT. In the adjusted regression model, HAMA score remained negatively associated with Valsalva ratio (B=-0.0368, p=0.001). The model had an R^2 of 0.220 and an adjusted R^2 of 0.131.

Conclusion: Greater anxiety severity was associated with a lower Valsalva ratio in newly diagnosed, untreated patients with essential hypertension. This association persisted after adjustment for selected demographic and anthropometric variables. However, the cross-sectional design does not establish causality and the findings require confirmation in larger studies.

Keywords: Essential hypertension; Anxiety; Hamilton Anxiety Rating Scale; Cardiovascular autonomic function; Valsalva manoeuvre; Cardiovagal function.

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INTRODUCTION

Hypertension is a major public health concern and an important risk factor for cardiovascular disease, stroke and premature mortality. Its development and progression involve interactions between genetic predisposition, environmental influences, metabolic factors and neurohumoral mechanisms. Among these mechanisms, the autonomic nervous system plays an important role in regulating heart rate, vascular tone and blood pressure. Alterations in sympathetic and parasympathetic activity have been implicated in the pathophysiology of essential hypertension.[1,2]

Cardiovascular autonomic function can be assessed using physiological tests that evaluate heart-rate and blood-pressure responses to specific stimuli. Commonly used tests include the heart-rate response to standing, heart-rate variation during deep breathing, the Valsalva manoeuvre, postural blood-pressure responses, sustained isometric handgrip and the cold pressor test. These tests assess different

aspects of cardiovascular reflex regulation and should be interpreted individually because they do not measure identical physiological responses.[3,4]

Psychological factors, including anxiety, may also influence cardiovascular regulation. Anxiety is associated with changes in emotional processing, physiological arousal and autonomic responses to stress. Persistent anxiety symptoms have been investigated in relation to sympathetic modulation and cardiovascular risk. Piccirillo et al. reported increased sympathetic modulation of heart rate at rest among hypertensive and normotensive individuals reporting anxiety symptoms.[5] These findings support a possible relationship between anxiety and cardiovascular autonomic regulation, although the strength and nature of this relationship may vary according to the population and the method used to assess autonomic function.

The Valsalva manoeuvre provides information about cardiovascular reflex responses to changes in intrathoracic pressure. The resulting changes in heart rate and blood pressure involve baroreflex mechanisms and other physiological processes.[3] Di Credico et al. reported that baroreflex sensitivity derived from the Valsalva manoeuvre predicted a lower anxiety response during exposure to carbon dioxide-enriched air in healthy adults.[6] Although their study differed from the assessment of anxiety severity in patients with hypertension, it provides related evidence of an association between baroreflex function and anxiety responses.

The Hamilton Anxiety Rating Scale is a clinician-administered instrument used to assess the severity of anxiety symptoms.[7] Examining HAMA scores alongside cardiovascular autonomic function tests may help clarify whether anxiety severity is associated with specific physiological responses in patients with essential hypertension. However, the relationship should not be assumed to be uniform across all autonomic parameters and an observed association does not necessarily establish a causal mechanism.

The present study was therefore undertaken to evaluate the association between anxiety severity and six cardiovascular autonomic function parameters in newly diagnosed, untreated patients with essential hypertension. By studying patients before antihypertensive treatment, the study sought to reduce the potential influence of medication on cardiovascular autonomic responses and to examine the relationship between anxiety severity and individual autonomic test results.

AIM AND OBJECTIVES

Aim: To evaluate the association between anxiety severity and cardiovascular autonomic function in newly diagnosed, untreated patients with essential hypertension.

Objectives:

1. To assess anxiety severity using the Hamilton Anxiety Rating Scale.
2. To evaluate cardiovascular autonomic function using the 30:15 ratio, Deep Breathing Test, Valsalva manoeuvre, Lying-to-Standing Test, Hand Grip Test and Cold Pressor Test.
3. To determine the correlation between HAMA score and each cardiovascular autonomic function parameter.
4. To assess the association between HAMA score and Valsalva ratio after adjustment for age, sex, BMI and WHR.

MATERIALS AND METHODS

Study Design

The present study was a cross-sectional analytical study conducted to investigate the association between anxiety severity and cardiovascular autonomic function in newly diagnosed, untreated patients with essential hypertension. The study was carried out in the Department of Physiology, Sardar Patel Medical College, Bikaner, Rajasthan, in collaboration with the Department of General Medicine, Kothari Medical and Research Institute, Bikaner, Rajasthan. The study included 50 patients with essential hypertension and focused on examining the relationship between anxiety severity and cardiovascular autonomic function in this population.

Study Population and Sample Size

The present analysis included 50 patients with newly diagnosed, untreated essential hypertension aged 36–55 years. The analysis focused on the relationship between anxiety severity and cardiovascular autonomic function within this hypertensive group.

Diagnostic Criteria

Hypertension was defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), using systolic blood pressure of 140 mmHg or higher and diastolic blood pressure of 90 mmHg or higher.[1] The diagnosis was based on repeated blood-pressure measurements and the absence of a secondary cause of hypertension.

Inclusion and Exclusion Criteria

Patients aged 36–55 years with newly diagnosed essential hypertension who had not received antihypertensive treatment and for whom HAMA and cardiovascular autonomic function data were available were included.

The exclusion criteria comprised diabetes mellitus, secondary hypertension, ischaemic heart disease or heart failure, chronic kidney disease, chronic liver disease, pulmonary tuberculosis, asthma or other chronic respiratory diseases, seizure disorders, arthritis affecting the performance of autonomic tests, pregnancy or lactation, current use of antihypertensive, psychotropic, or other medications that could influence autonomic function, severe psychiatric illness requiring active treatment, and

unwillingness or inability to cooperate with the study procedures.

Clinical and Anthropometric Assessment

Demographic and clinical variables included age, sex, BMI, WHR, systolic blood pressure, diastolic blood pressure, pulse pressure and pulse rate. Height and weight were measured, and BMI was calculated as weight in kilograms divided by the square of height in metres. Waist and hip circumferences were measured to calculate WHR.

Blood pressure was measured using a mercury sphygmomanometer after five minutes of seated rest, with an appropriately sized cuff. Two readings were obtained five minutes apart, and the average was used for analysis. Systolic and diastolic pressures were identified using Korotkoff phases I and V, respectively. Pulse pressure was calculated as systolic blood pressure minus diastolic blood pressure.

Assessment of Anxiety Severity

Anxiety severity was assessed using the Hamilton Anxiety Rating Scale, a clinician-administered instrument comprising 14 items. Each item is scored from 0 to 4, giving a total possible score of 0–56; higher scores indicate greater anxiety symptom severity.[7] The total HAMA score was used as the anxiety measure for correlation and regression analyses.

Cardiovascular Autonomic Function Tests

Six cardiovascular autonomic function tests were assessed. The 30:15 ratio was calculated from the heart-rate response following standing, using the longest R–R interval around the 30th beat and the shortest R–R interval around the 15th beat. The Deep Breathing Test assessed heart-rate variation during controlled deep breathing at six breaths per minute, expressed as the expiratory-to-inspiratory ratio. During the Valsalva manoeuvre, participants exhaled against a manometer at approximately 40 mmHg for 15 seconds; the Valsalva ratio was calculated from the longest R–R interval after release divided by the shortest R–R interval during the manoeuvre.

The Lying-to-Standing Test assessed the blood-pressure response to the change from supine to standing posture, including the fall in systolic blood pressure. The Hand Grip Test assessed the diastolic blood-pressure response to sustained isometric contraction at 30% of maximal voluntary contraction for three minutes. The Cold Pressor Test assessed the blood-pressure response to immersion of one hand in cold water at approximately 4–6°C for one minute.

Statistical Analysis

Correlation analysis was performed to examine the association between HAMA score and the six cardiovascular autonomic function parameters. Multiple linear regression analysis was performed to evaluate the association between HAMA score and Valsalva ratio, adjusting for age, sex, body mass index and waist-to-hip ratio. The correlation coefficients, regression coefficients, coefficient of determination (R^2), adjusted R^2 and corresponding p-values were used to interpret the findings. A p-value of less than 0.05 was considered statistically significant**.**

RESULTS

Clinical and Anxiety Characteristics

The study included 50 newly diagnosed, untreated patients with essential hypertension aged 36–55 years. The mean age was 41.26 ± 4.43 years, and the mean BMI was 27.15 ± 3.29 kg/m². The mean systolic blood pressure was 167.76 ± 14.11 mmHg, the mean diastolic blood pressure was 99.20 ± 7.99 mmHg, and the mean HAMA score was 9.38 ± 2.81.

Correlation Between Anxiety Severity and Cardiovascular Autonomic Function

Correlation analysis was performed to assess the relationship between HAMA score and each cardiovascular autonomic function parameter.

Table 1. Correlation between HAMA score and cardiovascular autonomic function parameters

Autonomic function parameter	Correlation coefficient (r)	p-value
30:15 ratio	+0.133	0.357
Deep Breathing Test	+0.232	0.105
Valsalva ratio	−0.415	0.003
Lying-to-Standing Test	−0.119	0.409
Hand Grip Test	−0.119	0.411
Cold Pressor Test	−0.070	0.630

A statistically significant moderate negative correlation was observed between HAMA score and Valsalva ratio (r=-0.415, p=0.003). This indicated that higher anxiety scores were associated with lower Valsalva ratios. No statistically significant correlations were observed between HAMA score and the 30:15 ratio, Deep Breathing Test, Lying-to-Standing Test, Hand Grip Test and Cold Pressor Test.

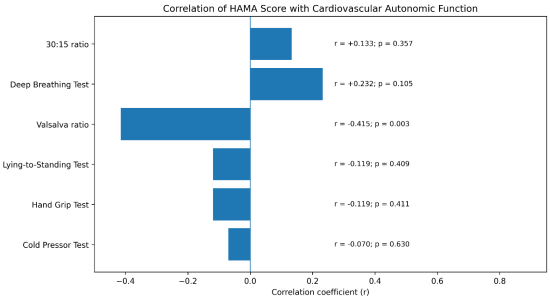
Multiple Linear Regression Analysis

Multiple linear regression was performed to assess the association between HAMA score and Valsalva ratio after adjustment for age, sex, BMI and WHR.

Table 2. Multiple linear regression model for Valsalva ratio

Model parameter	Result
R^2	0.220
Adjusted R^2	0.131
F-statistic	2.483
Overall model p-value	0.046
HAMA regression coefficient (B)	−0.0368
HAMA p-value	0.001
HAMA 95% confidence interval	−0.059 to −0.015

The overall regression model was statistically significant (F=2.483, p=0.046) and explained 22.0% of the variation in Valsalva ratio, with an adjusted R^2 of 0.131. HAMA score remained significantly negatively associated with Valsalva ratio after adjustment for age, sex, BMI and WHR (B=-0.0368, p=0.001). This indicated that higher anxiety scores were associated with lower Valsalva ratios after accounting for the covariates included in the model.



DISCUSSION

The present study evaluated the association between anxiety severity and cardiovascular autonomic function in 50 newly diagnosed, untreated patients with essential hypertension. The principal finding was a statistically significant moderate negative correlation between Hamilton Anxiety Rating Scale (HAMA) score and Valsalva ratio (r=-0.415, p=0.003). This association remained statistically significant after adjustment for age, sex, body mass index (BMI), and waist-to-hip ratio (WHR) (B=-0.0368, p=0.001). In contrast, no statistically significant correlations were observed between HAMA score and the 30:15 ratio, Deep Breathing Test (DBT), Lying-to-Standing Test (LST), Hand Grip Test (HGT) and Cold Pressor Test (CPT). These findings suggest that anxiety severity was associated with a specific measure of cardiovascular autonomic function rather than showing a consistent relationship across all the autonomic parameters examined.

The significant negative association between HAMA score and Valsalva ratio indicates that participants with higher anxiety scores tended to have lower Valsalva ratios. The Valsalva manoeuvre produces characteristic cardiovascular responses to changes in intrathoracic pressure and involves baroreflex-mediated regulation of heart rate and blood pressure. The Valsalva ratio is commonly used to assess cardiovagal function, although the response depends on the integrity of the broader cardiovascular reflex pathway and the performance of the manoeuvre.[3] The association observed in the present study may therefore indicate a relationship between anxiety severity and cardiovascular reflex regulation in patients with essential hypertension. However, the cross-sectional design does not establish whether anxiety contributes to altered autonomic responses or whether both are influenced by other physiological or psychological factors.

Previous research has also examined the relationship between anxiety and cardiovascular autonomic regulation. Piccirillo et al. investigated autonomic modulation of heart rate and blood pressure in hypertensive and normotensive participants with and without anxiety symptoms.[5] Their findings suggested that anxiety symptoms were associated with differences in cardiovascular autonomic modulation, supporting a possible link between psychological state and cardiovascular regulation. The present study is broadly consistent with this concept, although the methods used to assess autonomic function differed. Piccirillo et al. employed spectral analysis of heart-rate and blood-pressure variability, whereas the present study used conventional cardiovascular autonomic function tests. Consequently, the current findings add evidence of an association between anxiety severity and the Valsalva ratio but do not establish that anxiety is associated with all aspects of autonomic regulation.

Related evidence is provided by Di Credico et al., who investigated the relationship between baroreflex sensitivity derived from the Valsalva manoeuvre and anxiety responses during exposure to carbon dioxide-enriched air in healthy adults.[6] Their findings suggested that baroreflex sensitivity was associated with the anxiety response to this experimental stressor. Although their population and assessment methods differed from those of the present study, their work supports the possibility of an interaction between baroreflex function and anxiety. In the present study, the negative correlation between HAMA score and Valsalva ratio similarly indicates that greater anxiety severity was associated with a lower Valsalva response. Nevertheless, these findings cannot be considered directly equivalent because Di Credico et al. investigated experimentally induced anxiety and baroreflex sensitivity, whereas the present study examined

anxiety severity in patients with established hypertension.

No statistically significant association was observed between HAMA score and either the 30:15 ratio or DBT. These tests assess heart-rate responses to standing and controlled deep breathing respectively and are commonly used to evaluate cardiovascular cardiovagal function. Ewing et al. demonstrated the value of using a battery of cardiovascular autonomic function tests rather than relying on an individual test to assess autonomic abnormalities.[4] The findings of the present study are consistent with the importance of interpreting individual autonomic tests separately. Although the Valsalva ratio was significantly associated with anxiety severity, the 30:15 ratio and DBT did not demonstrate statistically significant relationships. This difference may reflect variation in the physiological responses assessed by the individual tests, biological variability, or the limited sample size. However, the present study cannot determine which of these explanation accounts for the observed pattern.

Similarly, HAMA score was not significantly correlated with LST, HGT and CPT. These tests evaluate cardiovascular responses to postural change, sustained isometric exercise and cold stimulation respectively. The absence of statistically significant correlations indicates that the study did not demonstrate a clear relationship between anxiety severity and these particular cardiovascular responses. This does not necessarily contradict research suggesting sympathetic activation in individuals with anxiety, because conventional cardiovascular responses to these tests are not interchangeable with direct measurements of sympathetic nerve activity or other indices of autonomic modulation. Chrysant investigated autonomic responses to handgrip, upright tilt and the Valsalva manoeuvre in patients with different forms of essential hypertension and reported differences in the responses obtained from these tests.[8] Although that study did not examine anxiety severity, it illustrates that individual autonomic tests may provide different information about cardiovascular regulation in hypertensive populations.

The multiple linear regression analysis further demonstrated that HAMA score remained negatively associated with Valsalva ratio after adjustment for age, sex, BMI and WHR. The regression coefficient (B=-0.0368, p=0.001) indicates that each one-point increase in HAMA score was associated with an estimated 0.0368-unit decrease in Valsalva ratio, with the other variables in the model held constant. The overall regression model was statistically significant (p=0.046), with an R^2 of 0.220 and an adjusted R^2 of 0.131. These results suggest that the association between anxiety severity and Valsalva ratio was not explained entirely by the measured demographic and anthropometric covariates included in the model. However, the adjusted R^2 indicates that a substantial proportion of the variation in Valsalva ratio remained unexplained. Other unmeasured factors may therefore contribute to differences in cardiovascular autonomic responses and statistical adjustment does not establish a causal relationship.

The inclusion of newly diagnosed, untreated patients with essential hypertension is an important feature of the present study because antihypertensive medication may influence cardiovascular autonomic responses. Studying untreated participants reduces this potential source of variation. The assessment of anxiety using HAMA, together with six cardiovascular autonomic function tests, also allowed the relationship to be examined across different physiological responses. Nevertheless, several limitations should be considered when interpreting the findings. The cross-sectional design precludes conclusions about causality or the direction of the association. The sample size of 50 participants may have limited the ability to detect smaller correlations. Furthermore, multiple correlations were examined, and the statistically significant finding should be interpreted with appropriate caution in view of multiple testing. The regression analysis also included a limited number of covariates, so residual confounding cannot be excluded. Finally, the findings may not be generalisable to all patients with hypertension or to the general population.

Overall, the present study demonstrated a significant negative association between anxiety severity and Valsalva ratio in newly diagnosed, untreated patients with essential hypertension and this association persisted after adjustment for age, sex, BMI and WHR. The findings are broadly consistent with previous research suggesting an interaction between anxiety and cardiovascular autonomic regulation, although differences in study populations and assessment methods limit direct comparisons. The absence of significant associations with the other five autonomic parameters suggests that the observed relationship may be specific to the cardiovascular reflex function reflected by the Valsalva ratio rather than indicating generalised autonomic dysfunction. Further studies involving larger samples and longitudinal assessment are needed to establish the reproducibility, underlying mechanisms and clinical implications of this association.

SUMMARY AND CONCLUSION

The present study evaluated the association between anxiety severity and cardiovascular autonomic function in 50 newly diagnosed, untreated patients with essential hypertension. A significant moderate negative correlation was observed between HAMA score and Valsalva ratio (r=-0.415, p=0.003) and this association remained significant after adjustment for age, sex, BMI and WHR. No significant correlations

were found between anxiety severity and the other five cardiovascular autonomic function tests.

In conclusion, greater anxiety severity was associated with a lower Valsalva ratio in patients with newly diagnosed, untreated essential hypertension. This finding suggests a possible relationship between anxiety and cardiovagal function; however, the cross-sectional design does not establish causality.

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