

ORIGINAL ARTICLE

Role of Serum Interleukin-6 as a Predictor of Left Ventricular Hypertrophy among Hypertensive Adults

JAHANZAIB MALIK¹, SALEH RASHEED², FAISAL TOHEED³¹Resident, Department of Medicine, Jinnah Hospital Karachi²Medical Officer, Liaquat Medical College / Jinnah Sindh Medical University, Karachi³Senior Registrar, Department of Cardiac Anaesthesia, Prince Sultan, Cardiac Center, Riyadh Saudi Arabia

Correspondence to: Saleh Rasheed, Email: Salehradhes034820844@gmail.com

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INTRODUCTION

One of the most common chronic cardiovascular diseases in the world is hypertension whose long-term effects continue to be a significant contributor to morbidity and mortality, especially in the low and middle-income nations¹. Continuous increases in the pressure of the arteries cause

ABSTRACT

Background: Hypertension is one of the biggest health problems in the world and it is closely linked to structural heart complications especially left ventricular hypertrophy (LVH). It has been found that chronic inflammation has become a primary cause of hypertensive end-organ damage, with Interleukin-6 (IL-6) a central mechanistic cause of this pathway. Nonetheless, regional statistics of Punjab and Pakistan in general are few.

Aim: To test the hypothesis that serum IL-6 is a predictor of LVH in hypertensive adult patients and to test the hypothesis that serum IL-6 relates to left ventricular mass index (LVMI).

Methods: The study involved a cross-sectional analytical study in tertiary care hospitals in Punjab, Pakistan, between June 2024 and May 2025. Hypertensive adults aged 30-70 years (n= 70) were enrolled. Clinical analysis, blood pressure, serum IL-6 (ELISA) and echocardiographic analyses of LVMI were conducted. LVH was considered to be LVMI greater than 115 g/m² in men and greater than 95 g/m² in women. Data analysis was done with independent t-tests, Pearson correlation, and multivariate logistic regression.

Results: LVH was found in 45.7 percent of the participants. The serum IL-6 levels were much higher in the people having LVH than in those with no LVH (12.14 ± 4.52 pg/mL vs. 6.02 ± 2.48 pg/mL; p = 0.001). A positive relationship was found between IL-6 and LVMI (r = 0.61, p < 0.001). Multivariate analysis also ensured that IL-6 was an independent predictor of LVH (AOR 3.74, 95% CI: 1.827.14), when adjusted readings were done by age, BMI, systolic BP and hypertension duration.

Conclusion: IL-6 levels are high predictors of LVH in hypertensive adults and can be a useful biomarker in the initial diagnosis of cardiac remodeling. Combining IL-6 measurement with the regular assessment of hypertension would improve the early risk stratification and clinical decision-making.

Keywords: Interleukin-6, hypertension, left ventricular hypertrophy, LVMI, inflammation, cardiovascular remodeling, biomarker.

gradual structural and functional modifications on the heart with the most remarkable change being the left ventricular hypertrophy (LVH)². LVH is a primary sign of host organ injury and is closely linked to an elevated risk of heart failure, arrhythmias, ischemic events, and sudden cardiac death³. Diagnosis of LVH at early stage is hence important

in avoiding chronic cardiovascular effects among hypertensive patients⁴.

Conventionally, the cause of LVH has been considered to be the result of hemodynamic overload which was due to long term hypertension⁵. Nevertheless, there is growing evidence to suggest that chronic low-grade inflammation has a significant mechanistic contribution to myocardial remodeling⁶. The Interleukin-6 (IL-6) is one of the most recent inflammatory mediators that are central to vascular dysfunction, endothelial activation, and hypertrophic signaling⁷. Immune cells, adipocytes, vascular smooth muscle and even cardiomyocytes secrete IL-6 and it has been reported to increase in hypertension, metabolic syndrome, obesity, and heart failure⁸.

The IL-6 enhances cardiac hypertrophy by activating intracellular pathways JAK/STAT3, MAPK, and NF- κ B, which induce cardiomyocyte growth, extracellular matrix deposition and fibrosis⁹. This has led to the interest of IL-6 being used as a possible biomarker to indicate the early inflammatory alterations that occur prior to structural cardiac remodelling¹⁰. Even though some of the studies based on Western populations indicate an association between high levels of IL-6 and LVH, there are still limited studies on South Asian populations where hypertension can show earlier and disease development is usually more virulent¹¹.

Since the burden of hypertension in Pakistan is high, and the prevalence of cardiovascular complications is growing, the necessity to investigate readily measurable biomarkers that can be used to predict LVH before it is too late to reverse the irreversible cardiac disease is high¹². Serum IL-6 is easy to measure and is minimally invasive and widely available, and could make a potential early risk stratification candidate¹³.

The aim of this research thus was to determine the relationship between the serum IL-6 and left ventricular hypertrophy in hypertensive adults¹⁴. In assessing the IL-6 as a predictive variable of structural heart alteration, this study will present evidence on the need to include the inflammatory biomarkers in regular monitoring of cardiovascular risks in hypertensive patients¹⁵.

MATERIAL AND METHOD

Study Design and Setting

It was a cross sectional analytical study that was carried out in various hospitals in Punjab, Pakistan which were tertiary care. This was an attempt to assess the relationship between serum Interleukin-6 (IL-6) concentrations and left ventricular hypertrophy (LVH) in individuals who already had known hypertension. The research environment also exposed the authors to a wide range of hypertensive patients that constituted both urban and semi-urban

communities, and it was sufficient to analyze clinical heterogeneity.

Study Duration

The research was conducted during an ongoing 12-month timeframe, between June 2024 and May 2025, which would be enough time to recruit and select participants, perform clinical monitoring and laboratory analysis, as well as echocardiography.

Study Population

The sample size was 70 of essential hypertension-diagnosed adults. The participants were aged 30 to 70 and were sampled at the participating 3rd party care tertiary care outpatient clinics and inpatient wards. Only those individuals that confirmed having hypertension at least one year were accepted. They were not to include patients who had ischemic heart disease, symptomatic heart failure, valvular heart disease, chronic kidney disease stage 3 or higher, active or chronic infections, autoimmune disorders, malignancy, or had steroid or immunosuppressive therapy. The pregnant women were also ruled out in order to exclude physiological confounders. Informed consent was given by all participants before their enrolment.

Clinical Assessment

A thorough clinical assessment was conducted on each participant, which included demographic profiling, body mass index (BMI) measurement, estimation of the duration of hypertension, and record of antihypertensive medication. Standardised clinical protocols were used to measure blood pressure, which was taken when a person was sitting in a comfortable position, and the mean of three results was taken in order to minimise error variation in measurements.

Laboratory Procedures

Samplings of the venous blood were taken against an overnight fasting. The serum was separated and kept at controlled conditions until it was analyzed. The level of serum IL-6 was analyzed using a calibrated enzyme-linked immunosorbent assay (ELISA), by the directions of the manufacturer. Each sample was subjected to two replications to enhance the level of accuracy and minimize the impact of errors in the analysis. The process relied on internal quality controls and calibration curves to make the results reliable.

Echocardiographic Evaluation

An experienced cardiologist conducted transthoracic echocardiography based on a standard imaging protocol. Measures of left ventricular dimensions and calculation of left ventricular mass (LVM) were done according to

Devereux-modified formula. The calculated LVMI was calculated by indexing the calculated LV to the body surface area. The cut-offs adopted to define LVH included LVMI more than 115 g/m² in men and more than 95 g/m² in women. The measurements were recorded to three cardiac cycles and averaged to make them consistent.

Data Quality Control and Management.

All clinical, laboratory and echocardiographic information was keyed into prepared proformas and then moved over to a secure electronic database. During the process of sample handling, and data entry, quality control measures were observed in order to reduce errors. Laboratory tests were done with proper internal controls and echocardiographic results were followed by internationally acceptable standards.

Statistical Analysis

Analysis was done using SPSS version 26 through statistical analysis. Continuous variables were given as the mean with the standard deviation, and frequencies and percentages were given as the categorical variables. The independent-sample t-tests were used to nominate the differences between serum IL-6 levels of groups with and without LVH. Pearson correlation coefficients were calculated to determine the relationship between LVMI and IL-6. Multivariate logistic regression analysis was used to identify whether or not IL-6 alone was a predictor of LVH after controlling age, sex, body mass index, systolic blood pressure and hypertension duration. All tests of statistics were taken to be statistically significant when the p-value was less than 0.05.

RESULTS

The study involved 70 hypertensive adults, the mean age of whom is 53.7 ± 9.8 years. Out of them, 41 (58.6) happened

to be females and 29 (41.4) to be males. The average time of hypertension was 8.4 years ± 4.1 years and the mean systolic blood pressure at entry was 149.2mmHg ± 17.5mmHg. Those 32 participants (45.7%), who had left ventricular hypertrophy (LVH), but 38 participants (54.3%), who did not have echocardiographic signs of LVH. Table 1 provides the baseline characteristics of the two groups.

The LVH participants had significantly higher levels of serum IL-6 than participants without LVH, but the mean values were 12.14 ± 4.52 pg/mL and 6.02 ± 2.48 pg/mL, respectively. This was found to be significantly different (p < 0.001) which implies that there is a close relationship between the state of inflammation and the structural alterations of the heart. Table 2 presents the full comparison of the laboratory parameters between the two groups.

There was a close and statistically significant positive relationship between serum IL-6 levels and left ventricular mass index (LVMI) (r = 0.61, p < 0.001). This implies that the higher the IL-6, the more the ventricular mass and the possibility of hypertrophy were more likely. The overview of the correlation analysis is presented in Table 3.

In multivariate logistic regression analysis, high IL-6 levels still served as an independent predictor of LVH after the age, gender, BMI, systolic blood pressure and hypertension duration had been accounted. The odds ratio (AOR) of IL-6 was adjusted (3.74) with a 95 percent confidence interval (1.827.14), which supported the fact that it is a strong predictive biomarker. Additional predictors of considerable importance were systolic blood pressure and years of hypertension. All the results of the regression are contained in Table 4.

All in all, it can be concluded that the level of serum IL-6 is highly predictive of hypertensive cardiac remodeling and may be used as an effective biomarker to predict LVH in hypertensive adults.

Table 1. Baseline Characteristics of Study Participants

Variable	LVH Present (n = 32)	No LVH (n = 38)	p-value
Age (years), mean ± SD	55.3 ± 10.1	52.4 ± 9.6	0.21
Gender (M/F)	15/17	14/24	0.42
BMI (kg/m ²), mean ± SD	27.8 ± 4.3	26.9 ± 3.8	0.38
Duration of Hypertension (years)	9.6 ± 4.5	7.4 ± 3.6	0.03*
Systolic BP (mmHg)	154.5 ± 16.8	145.2 ± 17.1	0.02*

Significant p-value <0.05

Table 2. Comparison of Serum IL-6 Levels Between LVH and Non-LVH Groups

Parameter	LVH Present (n = 32)	No LVH (n = 38)	p-value
Serum IL-6 (pg/mL)	12.14 ± 4.52	6.02 ± 2.48	<0.001*
LVMI (g/m ²)	132.8 ± 18.9	87.6 ± 12.7	<0.001*

Highly significant p-value <0.001

Table 3. Correlation Between Serum IL-6 and LVMI

Variables	Correlation Coefficient (r)	p-value
IL-6 vs. LVMI	0.61	<0.001*

Strong positive correlation

Table 4. Multivariate Logistic Regression Predicting LVH

Predictor Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Serum IL-6	3.74	1.82–7.14	<0.001*
Systolic BP	1.28	1.02–1.61	0.04*
Duration of Hypertension	1.39	1.07–1.89	0.03*
Age	1.05	0.98–1.11	0.15
BMI	1.07	0.92–1.21	0.21
Gender	0.89	0.42–1.76	0.72

Independent predictors shown by significant p-values

DISCUSSION

The current investigation examined the association between serum Interleukin-6 (IL-6) and left ventricular hypertrophy (LVH) in hypertensive adults visiting tertiary care hospitals in Punjab, Pakistan¹. These results are good proofs that IL-6 is an important factor in the development of hypertension-related cardiac remodeling². The IL-6 levels were significantly higher in the participants with LVH than in those without LVH and the difference was significant³. This confirms the hypothesis that chronic, low-grade inflammation is not only a secondary effect but one of the primary cause factors of myocardial hypertrophy⁴.

The positive relationship between LVMI and IL-6 is also strong and positive⁵, which has also contributed to the biological plausibility of the relationship. It has been established that IL-6 can affect the growth of cardiomyocytes, the activation of fibroblasts, and the deposition of extracellular matrices via the JAK/STAT3, MAPK, and NF- κ B pathways⁶. These signaling cascades have been consistently associated with structural cardiac alterations particularly concentric hypertrophy⁷. High IL-6 concentration can thus be an indicator of an active inflammatory process, which hastens myocardial remodelling in hypertensive patients, prior to the onset of clinical manifestations⁸.

Multivariate logistic regression showed that IL-6 was an independent predictor of LVH even after the age, BMI, systolic blood pressure and duration of hypertension were taken into account⁹. This observation is especially relevant since conventional factors of LVH, including pressure overload and the duration of the disease, do not completely account for the differences of cardiac remodeling that are observed in hypertensive individuals¹⁰. The independent correlation of IL-6 indicates that there is inflammatory processes that add additional predictive prospects to hemodynamic factors¹¹.

These findings are in line with already published international research studies that have also indicated

increased levels of IL-6 in the patients with hypertensive heart disease and LVH¹². Nevertheless, the given study introduces new data on a South Asian population, in which the load of hypertension is significant, and the emergence of cardiovascular issues is often a common occurrence¹³. Local data are valuable to enhance the risk stratification of Pakistani hypertensive patients due to the regional variation in the genetics, diet, lifestyle, and access to healthcare¹⁴.

The other significant implication of this research is that IL-6 is also a potential biomarker that is easy to measure to determine high-risk patients¹⁵. Though the gold standard method of the detection of LVH, echo cardiography is not always available in resource constrained environments¹⁶. Conversely, serum IL-6 assay is low-cost, non-invasive and general¹⁷. The IL-6 may be used as a supplement to conventional hypertension monitoring to enable clinicians to identify early myocardial changes and take prompt intervention before it is too late¹⁸.

Although there are the strengths of interpretation, a number of limitations are to be noted¹⁹. The cross-sectional design fails to enable the determination of causality between increase in IL-6 and the development of LVH. Although the sample size is sufficient to analyse the data, broad generalization is not possible because of a small sample size. Further, some other inflammatory markers to include CRP, TNF-alpha, and IL-1B were not done, which may have given a more detailed profile of inflammation. The presented study has however been statistically demonstrated as having strong associations throughout oxygen which have in turn led to the relevance of IL-6 in hypertensive cardiac remodelling and has further pointed out its relevance in clinical evaluation²⁰.

CONCLUSION

The present paper has shown that serum IL-6 levels are highly increased in hypertensive adults with left ventricular hypertrophy proven through echocardiography. The IL-6 is

found to have a close association with the left ventricular mass index, and even upon correcting the conventional risks of the cardiovascular system, the IL-6 is an independent predictor of LVH. These results highlight the value of systemic inflammation in the etiology of hypertensive heart disease and indicate that IL-6 can be a useful biomarker to allow the detection of high-risk patients at an early stage.

Regular IL-6 measurements may help clinicians identify subclinical cardiac alterations, better risk stratification, and initiate therapeutic interventions. These findings should be confirmed by future longitudinal studies that involve bigger sample sizes to examine the use of IL-6-target therapies in the prevention or delay in progression of LVH.

DECLARATION

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Conflicts of interest: None declared

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