

**ORIGINAL RESEARCH**

# Correlation between serum liver enzymes and hypertension

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**ABSTRACT**

**Background:** The increasing prevalence of non-communicable diseases (NCDs), particularly hypertension, poses a global health challenge. Hypertension is a significant risk factor for cardiovascular diseases and stroke, with emerging evidence suggesting its association with liver dysfunction. Elevated liver enzymes such as ALT, AST, and ALP are potential markers of non-alcoholic fatty liver disease (NAFLD) and related conditions, which may contribute to hypertension's pathophysiology. This study aims to estimate serum liver enzyme levels in hypertensive and normotensive individuals and evaluate the correlation between serum liver enzymes and hypertension. **Materials and Methods:** A hospital-based cross-sectional study was conducted at B.L.D.E (DU) Shri B.M. Patil Medical College with 140 participants, divided into hypertensive and normotensive groups. Liver enzyme levels were measured alongside other clinical parameters. Inclusion criteria included individuals aged  $\geq 18$  years with no history of hepatotoxic drug use or severe liver disease. Data were analyzed using SPSS v20, employing t-tests, Mann-Whitney U tests, and Chi-square tests to compare groups. A p-value  $< 0.05$  was considered statistically significant. **Results:** The mean age of participants was  $55.66 \pm 11.1$  years, with a majority being male. Routine blood parameters did not differ significantly between groups. However, hypertensive individuals exhibited significantly higher mean levels of ALT, AST, and ALP ( $p < 0.05$ ) compared to normotensive participants. **Conclusion:** The study highlights a significant association between elevated liver enzymes and hypertension, suggesting liver dysfunction's potential role in hypertension's pathophysiology. Integrating liver enzyme assessments in hypertension management may provide insights into underlying mechanisms and identify individuals at risk for liver-related complications. Further studies are warranted to validate these findings and their clinical implications.

**Keywords:** Hypertension, Liver Enzymes, ALT, AST, ALP, Non-communicable Diseases, NAFLD

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**INTRODUCTION**

In the past, the world has faced challenges as complex as those now ascribed by a trio of threats: First, the undernourished and the unfinished agenda of infections; second, the increasing global burden of non-communicable diseases; and third, the complications arising from globalisation itself, like the ill-effects of climate changes.<sup>1</sup> Before the antibiotic era, communicable diseases had a dominant role, but with the advent of new efficient antibiotics, communicable diseases are now no more a big problem.<sup>2</sup>

Since there is an increase in the prevalence of diseases such as stroke, cardiovascular diseases, hypertension, diabetes, and cancer, non-communicable diseases are now projected as a global health crisis. The world health organisation's global status report (2010) states that non-communicable diseases are the leading cause

of worldwide deaths contributing to 60%.<sup>3</sup> In India, the situation is bleak. In 2005, total mortality of 53% and 44% of daily adjusted life years lost was attributed to non-communicable diseases. By 2030, the total mortality by non-communicable diseases is projected to be 67% in India.<sup>1,4</sup>

The alarming rise in the magnitude of non-communicable diseases demands urgent attention. Recently, the world health organisation identified six risk factors for non-communicable diseases for death and those six risk factors are hypertension; impaired glucose tolerance; tobacco usage; dyslipidemia; lack of physical activity and obesity.<sup>1</sup> Of the above-said risk factors, hypertension is responsible for 13% of total deaths in the world, followed by tobacco usage (9%); impaired glucose tolerance (6%); physical inactivity (6%), and obesity (5%).<sup>5</sup> Among the non-communicable diseases, hypertension claims a

number of first because of the following reasons; the most common chronic condition, a significant risk factor for heart disease and stroke, accounts for most drug prescriptions, and throughout the world, it is the number one attributable risk for deaths. Hypertension is one of the main components of a crucial metabolic syndrome. Metabolic syndrome, if present in an individual, increases the risk of cardiovascular diseases.

The liver, which is a vital organ, has numerous functions such as synthesis, storage, degradation and biotransformation of bio-molecules in the human body.<sup>6</sup> The association of the development of hypertension with liver dysfunction is being increasingly recognised.<sup>7,8</sup>

The liver enzymes - alanine and aspartate aminotransferase (ALT and AST),  $\gamma$ -glutamyl transferase (GGT), and alkaline phosphatase (ALP) are being widely used as markers of liver function. The elevated levels of ALT, AST, and GGT point out to excess fat deposition in the liver, a condition termed non-alcoholic fatty liver disease (NAFLD).<sup>9</sup> These enzymes have been considered to have substantial clinical and epidemiological importance as convenient, reliable markers of NAFLD and related liver dysfunction. Some epidemiological studies have shown an association between ALT and GGT with metabolic syndrome, cardiovascular diseases and type 2-diabetes. In previous studies, cardiovascular diseases have been shown to be the leading causes of death in NAFLD, with higher rates coinciding with increased liver-related mortality throughout follow-up investigations.<sup>10-12</sup>

Since hypertension happens to be a significant risk factor for both cardiovascular diseases as well as stroke, there should be a well-devised approach to knowing the factors involved in the pathogenesis and preventing hypertension. Hence, it is necessary to study the levels of liver enzymes in hypertensive people to know the correlation between serum liver enzymes and blood pressure for future intervention to control the elevation in blood pressure even after initiation of pharmacological therapy.<sup>13</sup>

## OBJECTIVE

The study's objective is to estimate the serum liver enzyme levels in randomly selected patients and to study the correlation of serum liver enzyme levels and hypertension.

## MATERIAL & METHOD

**Source of data:** The information for the study was collected from OPD and IPD patients in B.L.D.E (DU) Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura-583106, Karnataka.

**Study design:** Hospital-Based cross-Sectional Study

### Sample Size:

Using G\*Power version 3.1.9.4 software for sample size calculation, The correlation between ALT and SBP ( $r=0.157$ ,  $p=0.049$ ), this study requires a total

sample size of 140, so to achieve a power of 99% for detecting a difference in Means: **Exact** - Correlation: Bivariate normal model with 1% level of significance.

### Inclusion criteria

- Aged above 18 years.
- Normotensive patients.
- Hypertensive patients – both newly diagnosed and known cases of essential hypertension.

### Exclusion criteria

- Patients with a history of hepatotoxic drug intake.
- Patients with diagnosed causes of secondary hypertension.
- Patients with severe chronic or acute evidence of liver diseases.

## DATA COLLECTION

A detailed pro forma was used to collect detailed history and to record the vital parameters, and measure the anthropometric indices. Body weight was recorded using a portable weighing machine and height was measured using a stadiometer, and blood pressure was recorded using a standardised mercury sphygmomanometer. The Institutional Ethical Committee approved the study. The subjects were explained the procedure, and informed consent was obtained. Detailed history was then be elicited from the subjects to exclude diabetes mellitus and renal causes to rule out the causes of secondary hypertension.

Weight was recorded in kilograms using a portable standard weighing machine and vertical height was measured in centimetres using a stadiometer and Quetelet's index was used to calculate body mass index (BMI):  $\text{weight}(\text{in kg})/\text{height}(\text{in m}^2)$

To begin with, the subjects were seated in a quiet room with a comfortable room temperature in an armed chair with the arm and back supported and the legs uncrossed. The mercury sphygmomanometer should be at his/her heart level. It is necessary that there should be abstinence from caffeine ingestion before 30 min of measurement of BP, and then using a standard sphygmomanometer having a cuff size of 25cm x 12.5cm, blood pressure was recorded two times by auscultatory method, and the mean value of the two measurements was taken for analysis. Blood was collected from the antecubital vein in front of the forearm after sterilising the skin with a sterilised cotton swab. About 5 ml of venous blood was drawn from each subject in a plain dry vacutainer tube using disposable syringes.

## STATISTICAL ANALYSIS

The data obtained is entered in a Microsoft Excel sheet, and statistical analyses are performed using a statistical package for the social sciences (SPSS) (Version 20). Results are presented as Mean, SD, counts and percentages, and diagrams, for normally distributed continuous variables between the two

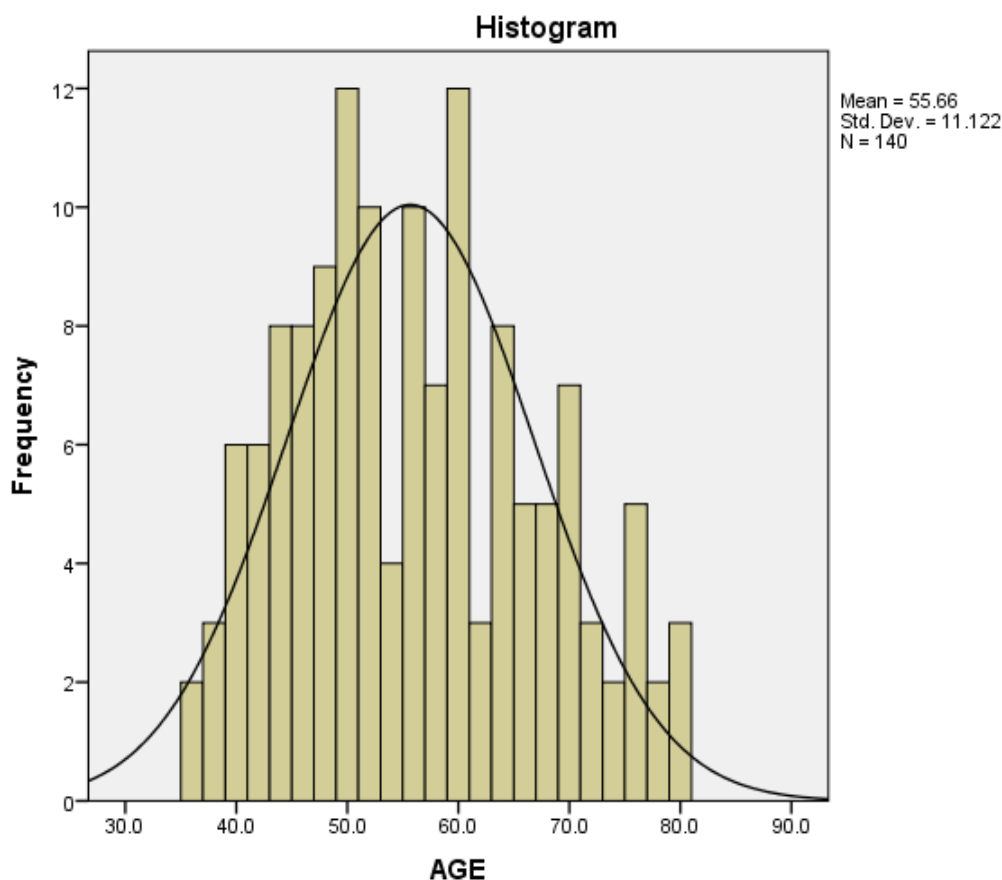
groups, will be compared using an independent sample t-test. For not normally distributed variables, the Mann-Whitney U test is used, for Categorical variables between the two groups are compared using the Chi-square test/Fisher's exact test. If  $p < 0.05$  will be considered statistically significant. All statistics are performed two-tailed

**RESULTS**

Table 1 provides information on the overall mean age of participants. Present study included total of 140 patients fulfilling inclusion criteria and separated into two groups with hypertension and without hypertension. The overall mean of the patients included was  $55.66 \pm 11.1$  yrs with minimum age of 36 years and maximum of 80 years with figure 1 depicting the same in form of a histogram.

**Table 1: Overall mean age of the participants**

	N	Minimum	Maximum	Mean	SD
Age	140	36.0	80.0	55.66	11.1

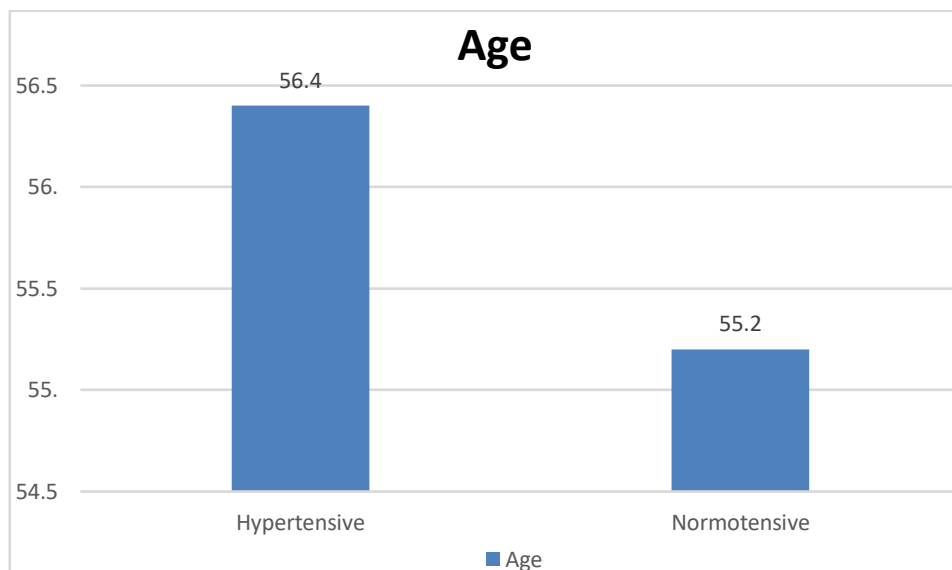


**Figure 2: Histogram showing Overall mean age of the participants**

Table 2 and figure 3 provide information on the mean age of patients between both hypertensive and normotensive groups with 56.4 years being the mean age for hypertensive patients and 55.2 years as mean age of normotensive patients. The mean age between the groups were comparable with no significant difference noted.

**Table 2: Comparison of mean age of patients between the groups**

	Hypertensive		Normotensive		P-Value
	Mean	SD	Mean	SD	
Age	56.4	10.9	55.2	11.3	0.95

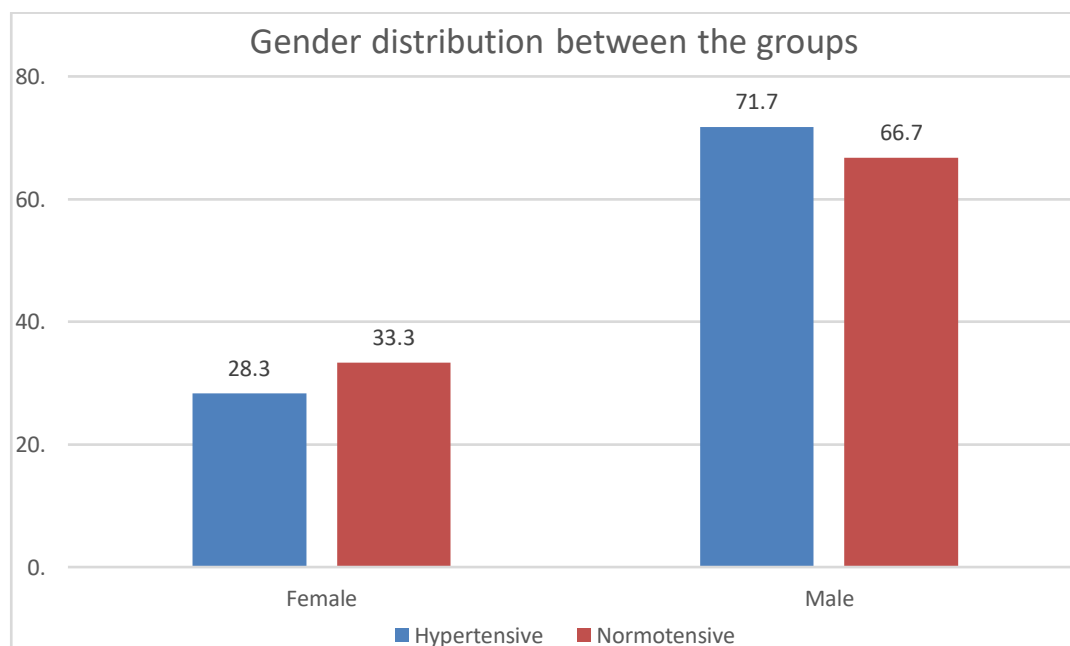


**Figure 3: Comparison of mean age of patients between the groups**

Table 3 and Figure 4 shows the gender distribution between both the groups. Hypertensive females accounted for 28.3%(15) where as males accounted for 71.7% (38) with total of 53 hypertensive patients and 87 normotensive cases. Among the participants, majority were males compared to female. The distribution of gender between the groups were comparable with no significant difference.

**Table 3: Gender distribution between the groups**

		Hypertensive		Normotensive	
		Count	N %	Count	N %
Sex	Female	15	28.3%	29	33.3%
	Male	38	71.7%	58	66.7%

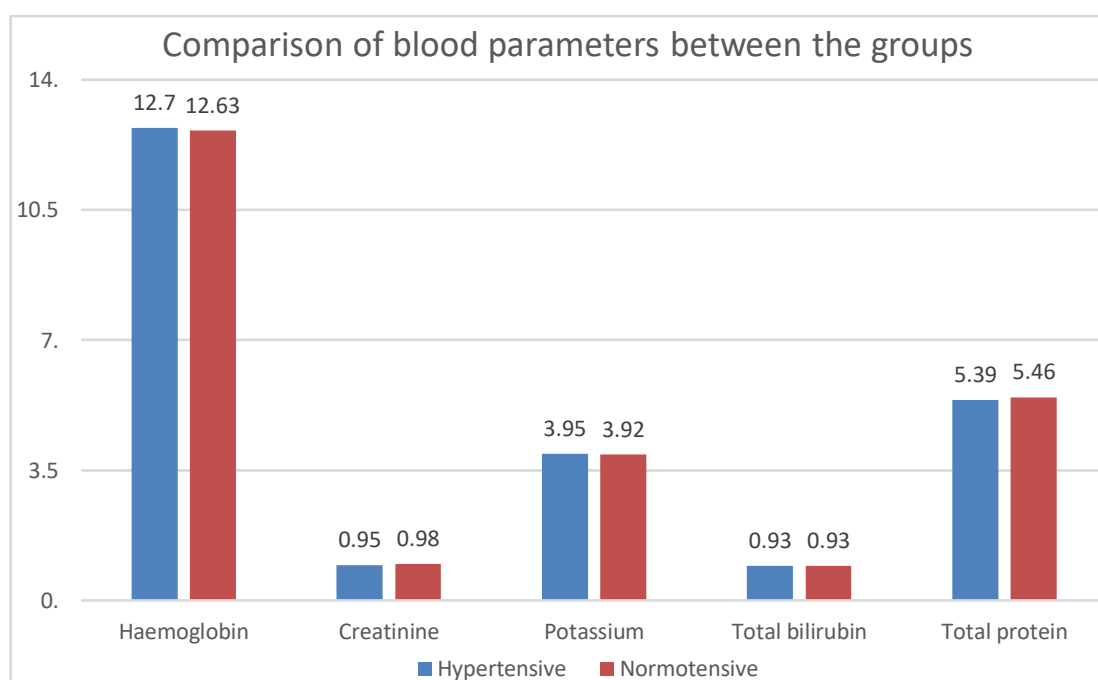


**Figure 4: Gender distribution between the groups**

Table 4 with figure 5 gives an overall picture of various blood parameters among both hypertensive and normotensive groups. On assessment of blood parameters, there is no significant difference noted in the mean haemoglobin, creatinine, serum sodium, potassium, total bilirubin and total protein levels between the groups.

**Table 4: Comparison of blood parameters between the groups**

	Hypertensive		Normotensive		P-Value
	Mean	SD	Mean	SD	
Haemoglobin	12.70	2.05	12.63	2.03	0.85
Creatinine	0.95	0.56	0.98	0.61	0.75
Sodium	139.75	7.91	139.49	7.92	0.85
Potassium	3.95	0.65	3.92	0.66	0.83
Total bilirubin	0.93	0.37	0.93	0.38	0.92
Total protein	5.39	0.62	5.46	0.62	0.54

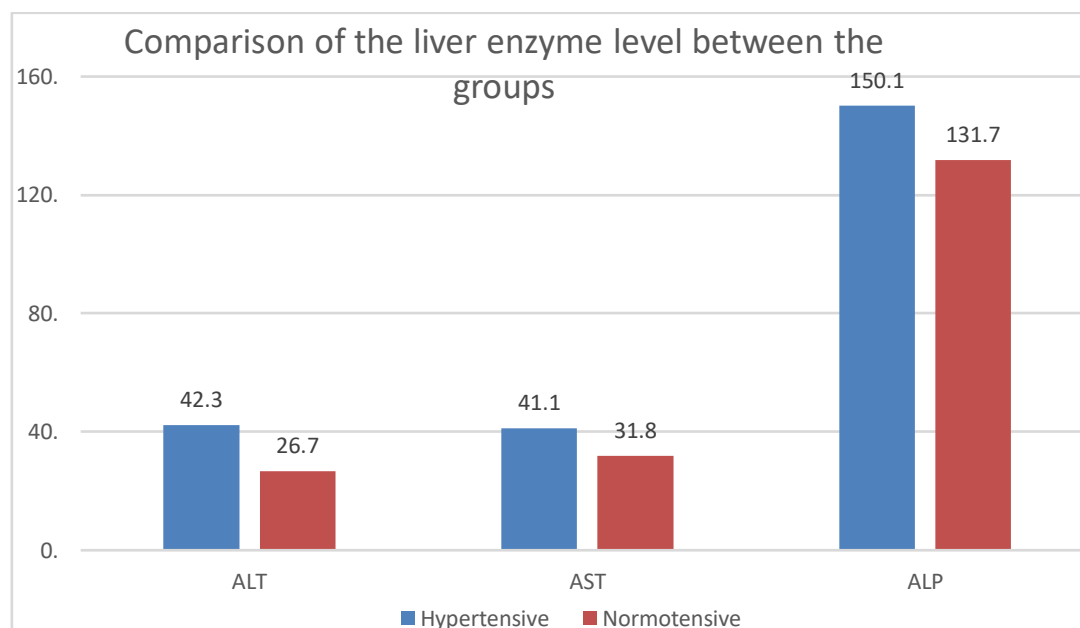


**Figure 5: Comparison of blood parameters between the groups**

Table 5 along with figure 6 compares the serum liver enzymes between the 2 groups – hypertensive and normotensive groups. On assessment of the liver enzymes, there was significant higher mean level of serum ALT, AST and ALP among the hypertensive patients compared to the normotensive individuals. ( $p < 0.05$ )

**Table 5: Comparison of the liver enzyme level between the groups**

	Hypertensive		Normotensive		P-Value
	Mean	SD	Mean	SD	
ALT	42.3	32.4	26.7	22.9	0.05*
AST	41.1	34.4	31.8	28.9	0.05*
ALP	150.1	65.6	131.7	58.4	0.05*



**Figure 6: Comparison of the liver enzyme level between the groups**

## DISCUSSION

Hypertension is a leading global health concern, contributing significantly to cardiovascular morbidity and mortality. While its etiology is multifactorial, emerging evidence suggests that liver function may play a role in the development and progression of hypertension. Serum liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), are markers of liver health and metabolic processes. Elevated levels of these enzymes have been linked to systemic inflammation, oxidative stress, and metabolic syndrome, all of which are potential contributors to hypertension. This study aims to investigate the correlation between serum liver enzyme levels and hypertension, providing insights into their potential role as biomarkers or therapeutic targets in hypertensive individuals.

Present study included total of 140 patients fulfilling inclusion criteria and separated into two groups with hypertension and without hypertension. The overall mean of the patients included was  $55.66 \pm 11.1$  yrs. The mean age between the groups were comparable with no significant difference noted. Among the participants, majority were males compared to female. The distribution of gender between the groups were comparable with no significant difference.

In similar, study by Khalili P et al., documented mean age of 49.94yrs with 46.56% were male patients.<sup>44</sup> Also in study by Rahman et al., majority of the participants were male compared to female with no significant difference in mean age between the groups.<sup>8</sup>

On assessment of blood parameters, there is no significant difference noted in the mean haemoglobin, creatinine, serum sodium, potassium, total bilirubin and total protein levels between the groups. On

assessment of the liver enzymes, there was significant higher mean level of serum ALT, AST and ALP among the hypertensive patients compared to the normotensive individuals. ( $p < 0.05$ )

In concordance to present study findings, Rahman S et al., documented with hypertensive group exhibited significantly higher mean concentrations of serum ALT, AST, and GGT compared to the normotensive group ( $p < 0.01$ ,  $p < 0.01$ , and  $p < 0.001$ , respectively). Elevated liver enzymes were more prevalent in the hypertensive group (49.2%) than in the normotensive group (38.1%), with a significantly higher prevalence of elevated ALT, AST, and GGT ( $p < 0.01$ ,  $p < 0.01$ , and  $p < 0.001$ , respectively). A clear trend of increased liver enzyme levels was observed with rising blood pressure, and serum ALT and GGT demonstrated an independent association with hypertension.<sup>8</sup>

Also in study by Khalili P et al., the higher levels of ALT, GGT, and ALP were associated with significantly increased odds of abnormal blood pressure.<sup>44</sup> Similarly Sakboonyarat B et al., found elevated serum AST and ALT levels were positively correlated with raised blood pressure (BP). Also, Hypertension was independently associated with higher odds of elevated AST and ALT in males, and elevated AST in females.<sup>46</sup> In line Baeradeh N et al., documented with Elevated levels of alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP) were significantly associated with an increased risk of hypertension, even after adjusting for potential confounding factors. Subgroup analyses also identified a notable relationship between ALP concentrations and high blood pressure within specific age ranges.<sup>47</sup>

Faramarzi E et al., study findings demonstrate that elevated levels of AST, ALT, ALP, and GGT are independently associated with pre-HTN (excluding ALP) and HTN, suggesting their potential utility as predictors for these conditions. Monitoring liver enzymes may enable primary care providers to identify at-risk individuals and implement timely interventions.<sup>48</sup>

McCallum L et al., study liver enzymes and bilirubin in hypertensive patients was within four standard deviations of the mean exhibited independent effects on mortality and blood pressure control. These findings highlight potential mechanisms linking liver markers to blood pressure and cardiovascular risk but provide limited support for their use in clinical risk stratification.<sup>41</sup>

### Recommendations

- 1. Routine Monitoring of Liver Enzymes:** Considering the significant link between elevated levels of serum ALT, AST, and ALP and hypertension, it is advised to incorporate liver enzyme assessments into the routine screening and ongoing care of hypertensive patients.
- 2. Integrated Care Approach:** Healthcare providers managing hypertension should adopt a collaborative approach, involving hepatologists or metabolic health specialists, to evaluate and address potential liver dysfunction or associated metabolic disorders when high liver enzyme levels are observed.
- 3. Lifestyle Modifications:** Hypertensive patients with elevated liver enzyme levels should be encouraged to adopt healthier lifestyle choices, such as following a nutritious diet, engaging in regular exercise, maintaining a healthy weight, and avoiding harmful substances like excessive alcohol, to enhance liver function and overall cardiovascular health.
- 4. Further Research:** Comprehensive, large-scale longitudinal studies are necessary to clarify the causal relationship between elevated liver enzymes and hypertension and to explore the underlying biological mechanisms connecting the two.
- 5. Risk Stratification:** Including liver enzyme levels in hypertension risk assessment models may help identify patients at a higher likelihood of developing complications, enabling healthcare providers to tailor management strategies more effectively.
- 6. Public Health Awareness:** Enhancing understanding of the relationship between liver health and hypertension among healthcare professionals and the general population is crucial for fostering early diagnosis and timely intervention.

### CONCLUSION

The findings of this study emphasize a noteworthy association between elevated serum liver enzyme levels and hypertension, suggesting that liver function may play a role in the pathophysiology of hypertension. While demographic and routine blood parameters showed no significant differences, the consistently higher levels of ALT, AST, and ALP in hypertensive individuals highlight the potential value of incorporating liver enzyme assessments into the clinical evaluation of patients with hypertension. This could aid in identifying individuals at risk of developing liver-related complications or uncovering underlying mechanisms linking liver health and hypertension. Further research is essential to confirm these findings and explore their clinical implications, but these results underscore the importance of a holistic approach to managing hypertension that considers liver function.

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