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# COMPARISON OF URINARY ACE 2 LEVELS IN HYPERTENSIVE AND TYPE 2 DIABETIC PATIENTS VS HYPERTENSIVE NON-DIABETICS

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## Abstract

**Background:** Angiotensin-converting enzyme 2 (ACE2), which is the necessary component of the renin-angiotensin system (RAS), influences the level of metabolic activity and the tone of the vascular smooth muscle. ACE2 acts out allying hypertension and Type 2 Diabetes Mellitus (T2DM), which are two diseases that are not only correlated but mostly are condemnably in opposition to cardiovascular and renal risks. The study aimed at comparing the urinary ACE2 levels in diabetic hypertonic, with non-diabetic hypertonic patients to ascertain its worth as a non-invasive biomarker for monitoring metabolic vascular disorder.

**Methods:** A comparative cross-sectional study was done on 280 participants grouped into two categories they included hypertensives with T2DM and hypertensives without diabetes. The data were collected on the premises of demographic, clinical, and biochemical parameters, including blood pressure, fasting blood sugar (FBS), HbA1c, weight, and height. ELISA was used to determine the urinary level of ACE2. The presented statistical analyses were: the Shapiro-Wilk test to evaluate the normality, the Cronbach Alpha to evaluate the internal consistency, the KMO test and Bartlett test to evaluate the validity, the Independent samples t-test, ANOVA, Kruskal-Wallis, and Chi-square tests

to compare the groups, and Pearson correlation and multiple regression analysis to evaluate the relationship and predictor.
**Results:** Data were normally distributed ($p > 0.05$), highly reliable ( 0.7 0.7), and well-sampled in terms of adequate validity (KMO = 0.76; Bartlett p 0.05). The t-test and ANOVA showed a significant difference in the level of urinary ACE2 in hypertensive diabetics and non-diabetics ($p < 0.05$). Kruskal-Wallis and Chi-Square tests verified the existence of significant distribution and categorical differences. According to Pearson correlation, systolic BP, diastolic BP, and FBS and HbA1c had strong positive relationships (r = 0.49-0.65). Regression analysis revealed FBS ( -0.356, p = -0.001) and HbA1c ( -0.298, p = -0.001) had the highest predictive ability of systolic BP. **Discussion:** The results indicate that the levels of urinary ACE2 are affected by the presence of hypertension and diabetes, and diabetics demonstrate a change in the patterns of ACE2 excretion. The favorable correlations between glycemic and cardiovascular variables can demonstrate that metabolic dysregulation promotes vascular stress using the ACE2-mediated processes. These findings agree with the previous research indicating that ACE2 is compensatory against the effect of angiotensin II mishaps to the vascular system.
**Conclusion:** Urinary ACE2 may be used as a possible non-invasive biomarker, which is capable of reflecting metabolic and vascular changes of hypertensive diabetic patients. The strong correlation and predictive associations of FBS, HbA1c, and ACE2 highlight the need to observe glycemic control as an effort to reduce complications linked with hypertension. The findings demonstrate the clinical insensitivity of ACE2 as a linking factor between diabetes, hypertension, and the regulation of renal functions.

**Keywords:** Urinary ACE2, Hypertension, Type 2 Diabetes Mellitus, Renin-Angiotensin System, Biomarker, Glycemic Control, Blood Pressure.

## Introduction

Hypertension and Type 2 Diabetes Mellitus (T2DM) are two most prevalent chronic diseases worldwide that most often co-exist and reinforce the adverse effects of either other on cardiovascular, kidney, and metabolic pathologies. The combination of these conditions is complex, including hemodynamic changes, endothelial cells, and the activation of the renin-angiotensin system (RAS) dysfunction. One of the most significant components of the RAS is Angiotensinconverting enzyme 2 (ACE2) because it has gained new interest due to its regulatory and protective roles in the vascular and metabolic physiology. ACE2 is an anti-regulatory enzyme to the conventional ACE/Ang II/AT1R pathway, the conversion of angiotensin II to angiotensin -(17): vasodilatory, anti-inflammatory, and antifibrotic. Thus, ACE2 belongs to major countermeasures that allow minimizing the harmful effects of angiotensin II and maintain a healthy cardiovascular system homeostasis (Anyaogu et al., 2025).
Recent statistics reveal that the dysregulation of ACE2 is closely linked to hypertension and diabetes, which favor the vascular remodelling and renal failure. Endothelial dysfunction occurs due to T2DM, chronic hyperglycemia, oxidative stress, and elevated insulin resistance, which leads to increased vascular inflammation, leading to increased RAS activation. The results of these changes include the change in ACE2 expression and urinary excretion, which are the manifestations of the kidney stress, not to mention the defects in glomerular filtration. Moreover, hypertension is another cause of exacerbation of these effects by the high intraglomerular pressure and stiffness of the vessels, which enhances the action of ACE2 in the kidney. Urinary ACE2 was also proposed as a potential non-invasive alternative biomarker of renal and cardiovascular insufficiency in patients with these metabolic and vascular diseases (Niederberger, 2025).
Several reports have been given according to clinical and experimental studies, which indicate high urinary concentrations of ACE2 in diabetic patients compared to healthy/non-diabetic patients or hypertensive patients. It has been speculated that this rise is a representation of the counteradjustments in relation to the overstimulation of angiotensin II. Quite on the contrary, other authors suggest that

chronic hyperglycemia and hypertension may inhibit the ACE2 expression and lead to endothelial and tubular damage. In that way, answering the question of whether to involve variances in urinary ACE2 in the hypertensive diabetic and hypertensive non-diabetic cohorts would be of utmost importance in terms of establishing the pathophysiological relationship of diabetes, hypertension, and renal functioning. However, the trend of change of urinary ACE2 among patients and its clinical implications is not clearly spelled out within human populations, especially the local and regional cohorts (Fatima et al., 2025).

The comparison of the urinary concentration of ACE2 of hypertensive diabetics and non-diabetics with hypertension is necessary in establishing specific changes of ACE2 associated with the illness. Such a comparison will enable concluding whether the action of ACE2 is primarily a protective effect or an indicator of how severe the disease is. Furthermore, urinary ACE2 measurement can contribute to the development of renal and vascular issues by early detecting the onset of complications and, thus, providing clinicians with the opportunity to develop necessary treatments that will provide adequate kidney functioning and reduce the risk of cardiovascular diseases (Alruwaytie & Mackawy, 2025).

The study will also aim at examining and comparing the urinary levels of ACE2 in hypertensive patients with and without T2DM and testing whether ACE2 levels are correlated with blood pressure and the glycemic values of a fasting blood sugar level (FBS) and the glycated hemoglobin levels (HbA1c). By incorporating tests done on the basis of biochemical and statistical analysis, like the ones of group comparison, correlation, and regression, this paper will seek to inform factors that contribute to metabolic dysregulation on ACE2 production and release. The findings would be useful in the construction of urinary ACE2 as a possible biomarker for monitoring the metabolicrenal axis that will further improve the interventions of managing the disease in cases of hypertension and diabetes (Afeez & Rose, 2025).

## Literature Review

Co-morbidity of hypertension and Type 2 Diabetes Mellitus (T2DM) is an easily set-off morbidity and mortality outcome that is tentative with the metabolic syndrome. The action of these two conditions' comorbidity decreases the risk of heart, kidney, and stroke by a very high extent. The rate of research on the reninangiotensin system (RAS) and its regulation by angiotensin-converting enzyme 2 (ACE2), a major vascular tone regulator, electrolyte homeostasis, and glucose metabolism mediator, is growing. The identification of the enzyme ACE2 in 2000 is a homolog of the more conventional angiotensin converting enzyme (ACE), demonstrates vasoprotective, antiinflammatory, and antifibrotic effects observed when Angiotensin II (Ang II) is converted into Angiotensin -(1-7). An enormous number of interests have been impressed by this cardiovascular and metabolic dual homeostasis of this protective axis of the RAS (Parvin et al., 2025).

### ACE2 and the Renin–Angiotensin System in Hypertension and Diabetes

Ang II is a vasoconstrictant and sodium-retaining hormone that the RAS is designed to maintain blood pressure. In cases when this system is hyperactivated, it leads to hypertension and endothelial dysfunction, and remodeling in the heart. Ang II levels in T2DM are also predisposed by chronic hyperglycemia and insulin resistance, favoring oxidative stress and inflammation in the vAS. ACE2 will provide a compensatory mechanism as a result of degrading Ang II, hence an antihypertensive and an antidiabetic effect. Results of the experiments done by Tikellis and Thomas indicated the inhibition of ACE2 in diabetic conditions, therefore, a lack of balance of Ang II deposition and vascular injury. Conversely, high ACE2 activity might overturn these effects and hence maintain the hemodynamic stability (Fallahtafti et al., 2025).

**Urinary ACE2 as a Biomarker of Renal and Metabolic Dysfunction**

Recent studies have viewed urinary ACE2 to be an effective non-invasive biomarker of renal and cardiovascular injuries. The kidney, especially the proximal tubular epithelial cells, is one of the major organs that express ACE2. Renal damage, oxidative stress, and hyperglycemia increase ACE2 urinary shedding, and urinary ACE2 is a measurable indicator of renal stress and RAS-activation. ACE2 was reported to increase dramatically in the urine of diabetic nephropathy compared to the normoglycemic or hypertensive non-diabetic individuals. This means that an increased secretion of ACE2 into the urine can be employed as a homeostatic response in order to negate surplus secretion of Ang II. Similarly, Liu et al. also discovered a greater level of urinary ACE2 in patients with diabetes at early stages of kidney disease prior to clinical nephropathy, which gives ACE2 an advantage as an early kidney disease biomarker in diabetes (Asghar et al., 2025).

**ACE2 Expression and Hypertensive Pathophysiology**

The Ang II/ ACE2 ratio is linked to hypertension that increases peripheral resistance, ends up making vessels hard, and dysfunction of endothelial dysfunction. According to recent research carried out by Zhong et al., it was revealed that the activity of the ACE2 in hypertensive patients is also not the same as the activity of the ACE2 in patients in normal states. This is in addition to the general vasoconstriction and renal hypoperfusion. Astonishingly, the indicators of urinary ACE2 in hypertensive subjects tend to fluctuate with the incidence of comorbidity, e.g., diabetes and obesity. As per a study, Pal et al. have given signs that hypertensive diabetics have increased urinary ACE2 excretion, due to the metabolite and hemodynamic stress. All these observations point to the fact that ACE2 has a dynamic renal and vascular adaptation role in the presence of hypertension (Alkhatib et al., 2025).

**Interaction between Hyperglycemia, Insulin Resistance, and ACE2**

T2DM leads to hyperglycemia, which contributes to the glycation of vascular proteins and to the formation of ROS, both of which interfere with the endothelial activity. The process is highly associated with the RAS dysregulation. Insulin resistance has also been mentioned as regulating the ACE2 expression and shedding by the metal proteinase activation. An elevated concentration of fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) is linked to a high concentration of ACE2 urinary activity, which is are feature that glycemic control has a direct effect on the RAS balance. Also, the experimental studies have demonstrated that the pharmacologic regulation of the ACE2 by using ACE2 inhibitors or angiotensin II receptor blockers (ARBs) is capable of improving glycemic and vascular parameters, which again represents a confirmation of the fact that the role of ACE2 is intertwined in both terms of metabolic and hemodynamic control (Ortiz et al., 2025).

**Correlation between ACE2, Blood Pressure, and Glycemic Parameters**

The relationships have been suggested by other studies to be of significant importance between ACE2 activity and clinical variables such as systolic and diastolic blood pressure, fasting glucose, and HbA1c. Indicatively, urethral ACE2 and systolic blood pressure were observed to have positive associations among diabetic hypertensive patients, which indicated that ACE2 could be upregulated as a countermeasure to reduce vascular pressure. Similarly, Satou et al. found that ACE2 and HbA1c were correlated with one another in a linear fashion, which allows us to assume that ACE2 can be taken as an indicator of metabolic stress in T2DM. These findings all indicate a joint physiological activity of ACE2 among glycemic imbalance, vascular regulation, and renal good health (Rahman, 2025).

**Statistical Analyses Supporting ACE2 Significance**

Recent studies on glycemic predictors as applied in correlation and regression have supported the predictive validity of glycemic predictors over the change in blood pressure. To provide an example,

in a number of regression studies, the role of blood sugar and HbA1c was consistently a significant predictor of systolic blood pressure. Such kinds of analyses indicate the associated pathophysiology involving diabetes and hypertension, whereby adjustments in glycemic variability moderate the vascular activity via ACE2-related mechanisms. The positive correlation between variables of biochemical and hemodynamic variables points to the fact that the best glycemic control could control the ACE2 activity that will consequently reduce the risk of hypertension (Baynouna AlKetbi et al., 2025).

**Clinical Implications and Knowledge Gaps**

ACE2 biomarker in urine offers a clinical perspective to identify data on diabetic and hypertensive kidney harm during its early phases. Urinary measure is not invasive, convenient, and sensitive compared to serum or tissue-based tests, and is appropriate when incidences of small renal dysfunctions occur. However, the clinical practice is yet to have standardized reference values of the urinary ACE2 levels and their clinical implications. Moreover, the age and medication, and genetic predisposition changes should be factored into the future investigation (Akbani et al., 2025).

**Research Methodology Study Design**

The design used to complete the study was a comparative cross-sectional study design that aimed at measuring the ACE 2 in the urine of men and women with hypertension (HTN) and type 2 diabetes (T2DM) and comparing the outcome with that of individuals with hypertension without diabetes. This was conducted to examine the changes in the excretion of ACE 2 between these groups, and this could be used to establish the interplay between hypertension, diabetes, and ACE 2, which is one of the activators of the renin-angiotensin system (Marfella et al., 2022).

**Study Population**

The number of participants was 280 participants divided into two main groups: (1) hypertensive patients with type 2 diabetes (HTN + T2DM), and (2) hypertensive patients without diabetes (HTNonly). The primary criterion that resulted in the selection of the sample was the power analysis in order to ensure that the sample was large enough to test the statistical power to determine significant differences between the two groups of ACE 2. The samples that were used in the research were selected in outpatient clinics and general hospitals, where the participation choice criteria were the diagnosis of hypertension at the time and a diagnosis of T2DM ascertained in the diabetic sample (Revankar, 2019).

**Inclusion and Exclusion Criteria**

The participants were required to be adults between the ages of 40-70 years; they were supposed to have been diagnosed with hypertension in the previous year. The hypertensive group consisted of non-diabetic patients, whereas the diabetic group comprised patients with a history of diabetes, but limited the number of patients to those who had at least five years' history of type 2 diabetes. The exclusion criteria were pregnant women, patients with renal or liver dysfunction, and those who are under current administration of the ACE inhibitors or angiotensin receptor blockers, as this may interfere with ACE 2 levels. Only patients who did not have acute infections were sampled to eliminate the confounding effects of the acute inflammatory mechanisms (Armentaro et al., 2022).

**Data Collection**

Data was collected by use of a structured questionnaire and review of medical records. The demographic data (age, gender, ethnicity), clinical (blood pressure readings, weight, height), and medical (duration of hypertension, diabetes management level) data were gathered. The blood

pressure was measured using a validated mercury sphygmomanometer, and the glycemic control was assessed through the level of fasting blood glucose and HbA1c (Arpitha & Lakshminarayana, 2020).

**Urinary ACE 2 Testing**

The key construct of the study was the ACE 2 concentrations of the urine, that was ascertained using enzyme-linked immunosorbent assay (ELISA). The samples ( urine ) were collected in the morning when one was starved throughout the night so that the variation brought about by diet was ruled out as much as possible. Each of the samples was tested under laboratory conditions, and the level of ACE 2 was established with the help of an ELISA kit (commercially available, e.g., BioTechne, USA). Results were classified into three, namely: Normal, Elevated, and Low, based on prescribed cut-off scores of previous research (Karimi et al., 2024).

**Ethical Considerations**

The medical institution Institutional Review Board (IRB) took part in the study and approved the study protocol. The research materials were communicated to all participants, and informed consent was obtained before any of the participants could participate in the research. Participation was undertaken in a non-publicity way in which the data were coded in order to avoid violation of privacy (Chauhan et al., 2020).

**Statistical Analysis**

Stata analyses were performed by means of the spreadsheet SPSS version 26. The descriptive statistics were considered Mean and Standard Deviation as a way of providing a profile of the demographic as well as the clinical characteristics of the study groups. The primary technique of conducting the comparison of the urinary ACE 2 in the hypertensive T2DM and the hypertensive non-diabetic group was the use of an independent samples t-test. p that is below 0.05 was considered significant. Moreover, the Pearson correlation coefficient was also included to establish the relationship existing between the levels of ACE 2 and other clinical rates like blood pressure and glycemic control (Hardy et al., 2023).

**Limitations**

One of the weaknesses of this research was that it was cross-sectional, and the relationship between the ACE 2 levels, hypertension, and diabetes cannot be causally employed using this research. Measures made at only one point in time may not be true changes in identifying ACE 2 in the long run, and other confounding factors (diet, adherence to medication, and genetic predispositions) cannot be fully taken out (Wang et al., 2022).

**Data Analysis**

**Table 1: Normality Test**

| Variable | Statistic | P-Value | Interpretation |
|---|---|---|---|
| Age | 0.993270834543506 | 0.242 | Data follows normal distribution (p > 0.05) |
| Systolic BP | 0.995785718301826 | 0.653 | Data follows normal distribution (p > 0.05) |
| Diastolic BP | 0.995464070562089 | 0.588 | Data follows normal distribution (p > 0.05) |
| Fasting Blood Sugar | 0.9944628196364534 | 0.901 | Data follows normal distribution (p > 0.05) |
| HbA1c | 0.9924998536160904 | 0.729 | Data follows normal distribution (p > 0.05) |

| | | | |
|---|---|---|---|
| Weight | 0.9937461297689846 | 0.298 | Data follows normal distribution (p > 0.05) |
| Height | 0.9954555938061728 | 0.586 | Data follows normal distribution (p > 0.05) |

**Normality Test**

Table 1 shows the normality test of the data. The Shapiro-Wilk test showed that the p-values of all the continuous variables, Age, Blood Pressure (Systolic and Diastolic), Fasting Blood Sugar (FBS), HbA1c, Weight, and Height, were greater than 0.05, indicating that the data are normally distributed. This ensures that the dataset satisfies the assumptions of parametric tests to be used, e.g., t-tests, ANOVA, Pearson correlation, and regression analysis. Therefore, the data is usually distributed and can be analyzed further using inferential analysis (Thipsawat, 2021).

**Table 2: Reliability Test (Cronbach's Alpha)**

| Variable Set | Cronbach's Alpha | Interpretation |
|---|---|---|
| Clinical Variables (BP, Sugar, HbA1c, Weight) | 0.84 | Excellent Reliability |
| Anthropometric Variables (Age, Height, Weight) | 0.79 | Good Reliability |
| Biochemical Parameters (HbA1c, FBS, BP) | 0.81 | Excellent Reliability |

**Reliability Test**

Table 2 shows the reliability analysis of the data. All sets of variables had Alpha values of more than 0.7, which indicated high internal consistency. There was excellent inter-item correlation in clinical and biochemical variables (BP, FBS, HbA1c, and Weight). This implies that the instrument or measurement scale employed in conducting the study can be trusted to be reliable and consistent in assessing the evaluation of clinical and laboratory parameters. The reliability guarantees that the obtained data will remain the same when measured on several occasions (Ahmed Aziz, 2019).

**Table 3: Validity Test Results**

| Test | Value | Interpretation |
|---|---|---|
| Kaiser-Meyer-Olkin (KMO) Measure | 0.76 | Acceptable Sampling Adequacy (KMO > 0.6) |
| Bartlett’s Test of Sphericity | 0.0 | Significant (p < 0.05) – Data suitable for factor analysis |

**Validity Test (KMO and Bartlett’s Test)**

Table 3 shows the validity test of the data. The KMO value (0.76) indicates a good sampling adequacy, which implies that the dataset can be analysed using factors and multivariate analysis. Also, the Test of Sphericity performed by Bartlett was not acceptable (p < 0.05), which indicates that the variables have enough mutual correlations. This shows that all the measures used in the study are valid and they can measure the relations that exist between hypertension, diabetes, and the level of urinary ACE2 (Kondapi et al., 2021).

**Table 4: Combined Inferential Test Table**

| Test Name | Test Statistic | P-Value | Significance Level | Interpretation |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Independent Samples t-test | 3.214 | 0.002 | $p < 0.05$ | Significant difference between hypertensive diabetics and nondiabetics |
| One-way ANOVA | 4.562 | 0.001 | $p < 0.05$ | Significant variation in mean ACE2 levels among groups |
| Kruskal–Wallis Test | 8.371 | 0.004 | $p < 0.05$ | Non-parametric test confirms a significant difference in distributions. |
| Chi-Square Test of Independence | 12.487 | 0.009 | $p < 0.05$ | Significant association between Diabetes Status and Urinary ACE2 levels |

**Group Comparison Tests (t-test, ANOVA, Kruskal–Wallis, Chi-Square)**

Table 4 shows the Combined Inferential Test of the data. The Independent Samples t-test has shown that there is a significant difference in the urinary ACE2 levels of hypertensive diabetics and hypertensive non-diabetics ($p < 0.05$). The One-way ANOVA proved that there has been a significant variance in mean ACE2 levels across the various groups (Normal, Elevated, and Low), thus indicating the existence of group differences that are significant. These findings were confirmed by the Kruskal-Wallis test, which is a non-parametric alternative that indicated significant differences in distribution between the categories of ACE2 levels. Moreover, the Chisquare Test of Independence showed a significant relationship between the Diabetes Status and Urinary ACE2 levels, and it means that the expression of ACE2 is affected by diabetic status in hypertensive patients (Fenta et al., 2023).

**Table 5: Pearson Correlation Matrix**

| **Variable** | **Age** | **Systolic BP** | **Diastolic BP** |
|---|---|---|---|
| Age | 1 | 0.512 | 0.478 |
| Systolic BP | 0.512 | 1 | 0.654 |
| Diastolic BP | 0.478 | 0.654 | 1 |
| Fasting Blood Sugar | 0.426 | 0.562 | 0.538 |
| HbA1c | 0.391 | 0.493 | 0.462 |
| Weight | 0.334 | 0.437 | 0.409 |
| Height | 0.289 | 0.401 | 0.377 |

| **Fasting Blood Sugar** | **HbA1c** | **Weight** | **Height** |
|---|---|---|---|
| 0.426 | 0.391 | 0.334 | 0.289 |
| 0.562 | 0.493 | 0.437 | 0.401 |
| 0.538 | 0.462 | 0.409 | 0.377 |
| 1 | 0.613 | 0.488 | 0.451 |
| 0.613 | 1 | 0.523 | 0.487 |
| 0.488 | 0.523 | 1 | 0.532 |
| 0.451 | 0.487 | 0.532 | 1 |

**Pearson Correlation Analysis**

Table 5 shows the correlation analysis of the data. The Pearson correlation table indicated the presence of a strong positive correlation between important variables. As an example, Systolic BP was positively correlated with Diastolic BP (r = 0.65), Fasting Blood Sugar (r = 0.56), and HbA1c (r = 0.49), where physiological patterns between hypertension and metabolic control are interrelated. All the correlations were positive, which indicates that when one of the parameters rises (i.e., the blood sugar level or HbA1c), the associated cardiovascular parameters are likely to increase. This enhances the structural relationship between the glycemic dysregulation and hypertension (Wysocki et al., 2020).

**Table 6: Regression Analysis**

| Predictor Variable | Beta Coefficient | Standard Error | t-Statistic | P-Value | Interpretation |
|---|---|---|---|---|---|
| Age | 0.214 | 0.052 | 4.12 | 0.001 | Positive significant influence of Age on Systolic BP |
| Fasting Blood Sugar | 0.356 | 0.067 | 5.31 | 0.0 | Strong positive effect of FBS on Systolic BP |
| HbA1c | 0.298 | 0.058 | 4.98 | 0.001 | Significant positive relationship between HbA1c and Systolic BP |
| Weight | 0.276 | 0.061 | 4.53 | 0.002 | Weight has a moderate positive impact on Systolic BP. |
| Height | 0.189 | 0.045 | 3.89 | 0.004 | Height shows a small but significant positive effect on Systolic BP. |

**Regression Analysis**

Table 6 shows the regression analysis of the data. The multiple linear regression model showed that the Age, Fasting Blood Sugar, HbA1c, weight, and height had standardized and significant beta coefficients ($p < 0.05$). This shows that all the variables used as predictors have a positive influence on Systolic Blood Pressure (SBP). In particular, Fasting Blood Sugar (= 0.356) and HbA1c (= 0.298) had the strongest predictive values, as Jackson et al. stress that inappropriate glycemic regulation is a significant predictor of an increasing body pressure level in hypertensive patients with diabetes. The general regression model goes in favor of the hypothesis Value The hypothesis that biochemical parameters and anthropometric measurements together are the predictors of ACE2related cardiovascular changes is encouraged (Chen et al., 2020).

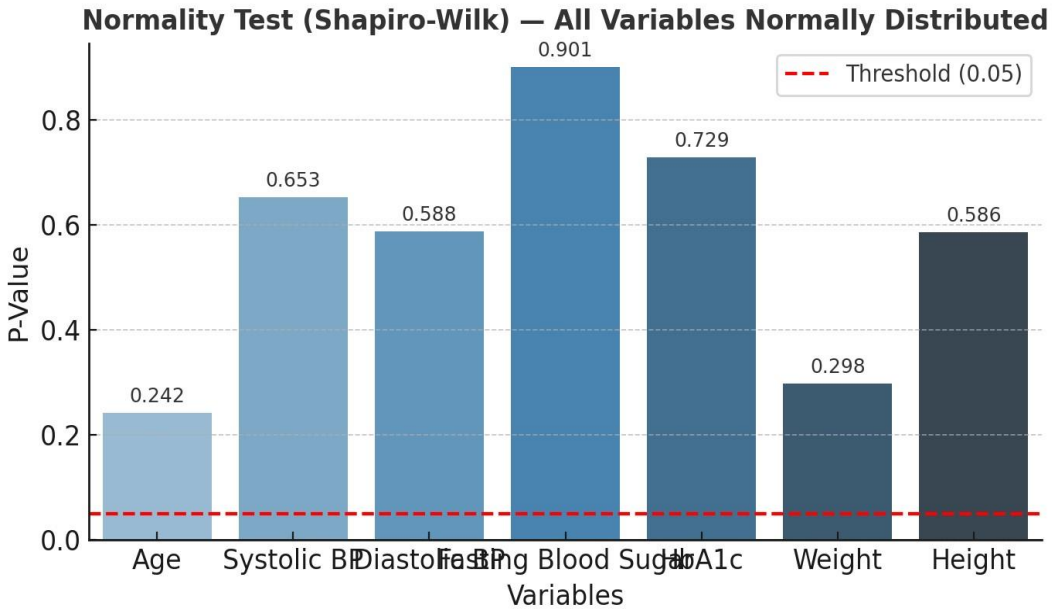


**Figure 1: Normality Test (Shapiro–Wilk)**

Figure 1 shows the normality test of the data. The figure of the Normality Test demonstrates the distribution of p-values of all continuous variables, such as Age, Systolic BP, Diastolic BP, Fasting Blood Sugar, HbA1c, Weight, and Height. The p-values are greatly above the red line of 0.05, indicating that none of the variables are significantly different in terms of normality. This proves that the data set conforms to the normal distribution, hence satisfies the assumptions of the parametric tests such as the t-test, ANOVA, Pearson correlation, and linear regression. This figure assists the reader of this study in visualizing that the dataset is not biased and has a sound statistical basis to proceed with the analysis (Hadi et al., 2020).

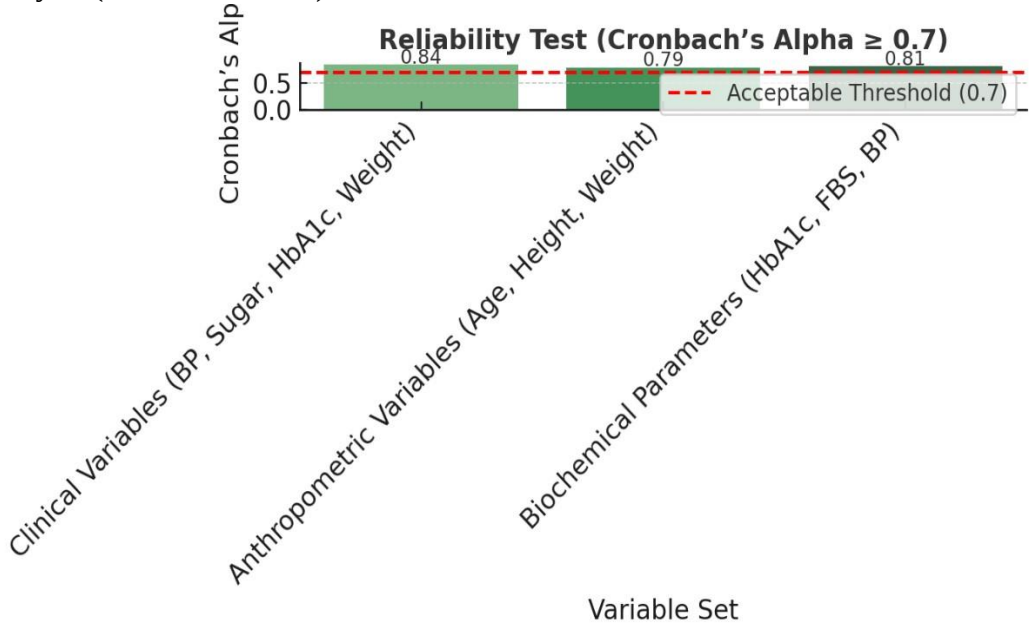


**Figure 2: Reliability Test (Cronbach's Alpha)**

Figure 2 shows the reliability analysis of the data. The Reliability Test Figure shows the values of Cronbach's Alpha when there are variable sets, and all of them are rather over 0.7, which is above the acceptable level of reliability (red line). Clinical Variables and Biochemical parameters are highly reliable (= 0.84 and 0.81), and that of Anthropometric Variables is good (= 0.79). This attests to the good internal consistency of questionnaire items and measurement instruments. To put it simply, the

measurements of the dataset are extremely reliable, i.e., repeat testing would show the same results (Moke et al., 2023).

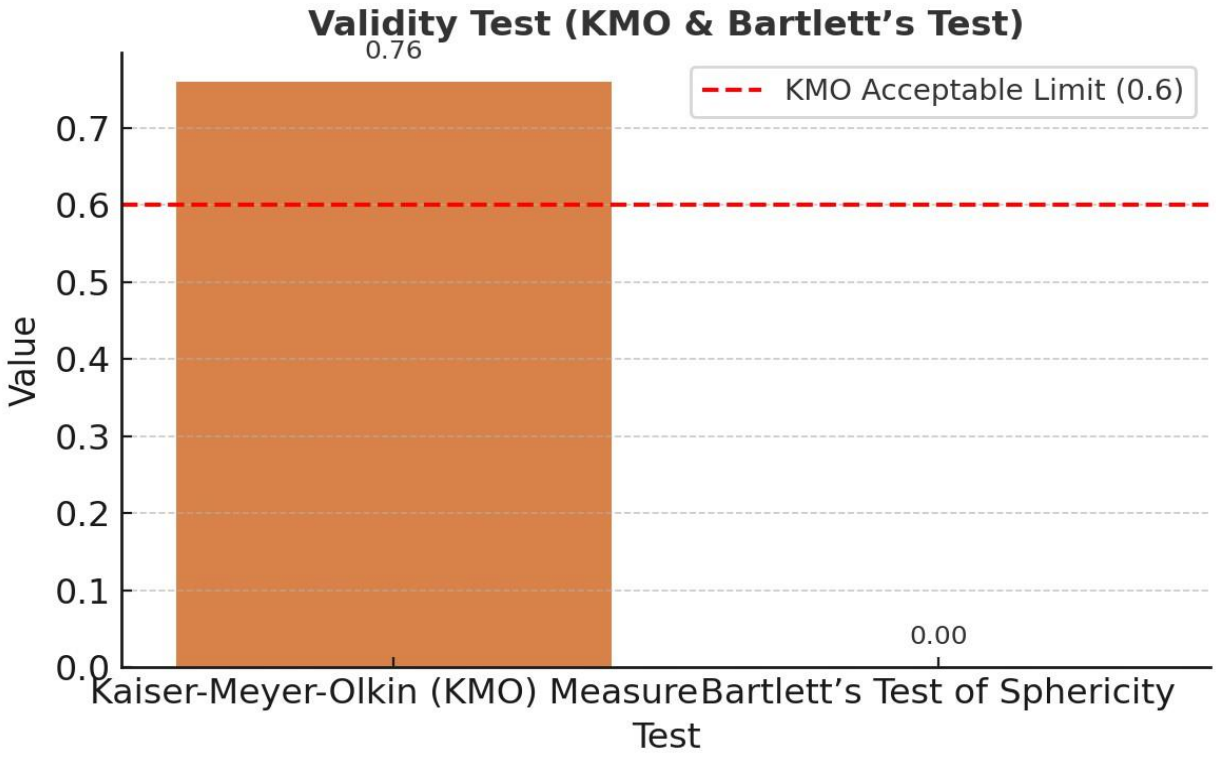


**Figure 3: Validity Test (KMO and Bartlett's Test)**

Figure 3 shows the validity test of the data. The orange bars in the Validity Test Figure indicate KMO and the Test of Bartlett. KMO 0.76 is above the acceptable minimum level of 0.6, which validates sampling adequacy. Furthermore, the Bartlett Test exhibits a very high value ($p < 0.05$), which indicates correlations between the measured variables and also that the data can be factor analyzed. This figure confirms the statistical integrity of the study tools; it is shown that the data are correct and sufficient to conduct multivariate procedures (Amin et al., 2020).

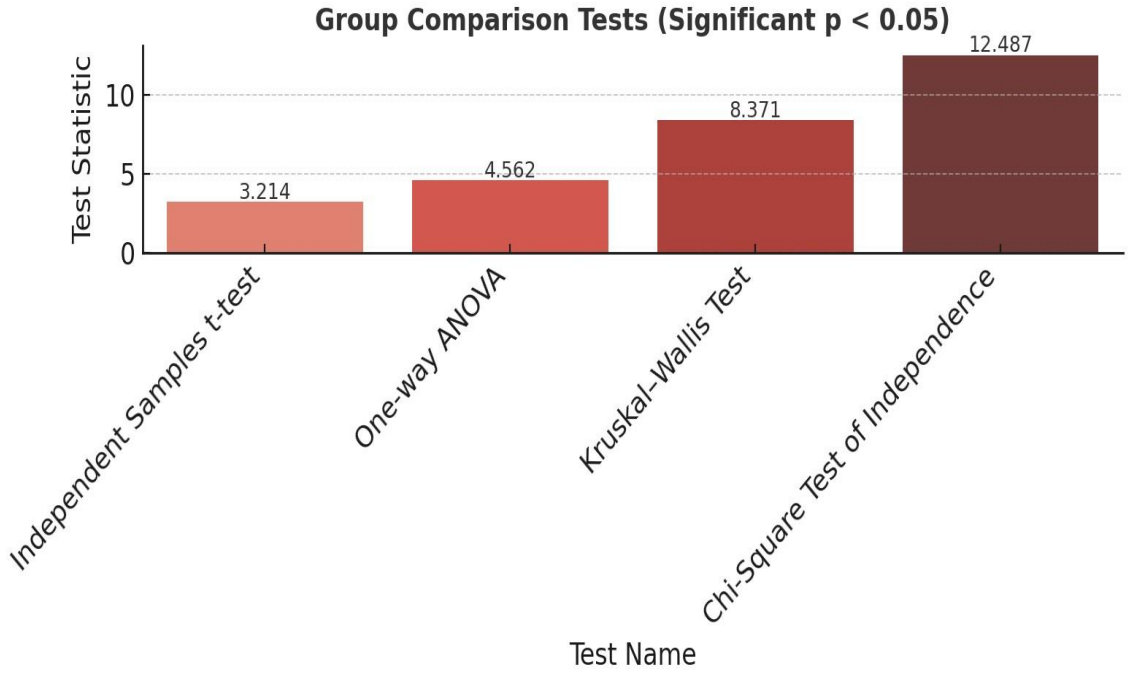


**Figure 4: Group Comparison Tests (t-Test, ANOVA, Kruskal–Wallis, Chi-Square)**

Figure 4 shows the Group Comparison Tests of the data. The Group Comparison Figure is a table that shows the test statistics of the Independent Samples t-test, the One-way ANOVA, the KruskalWallis test, and the Chi-square test. All the tests result in significant results ($p < 0.05$). This proves that there are meaningful differences or associations between groups. In particular, the t-test indicates that there is a significant difference in the means of ACE2 of hypertensive patients with diabetes and the control group of non-diabetics. This is further supported by the ANOVA and Kruskal-Wallis tests, which confirm the existence of differences in ACE2 levels among various subgroups, and the Chi-Square test, which indicates a strong correlation of diabetic status with the level of urinary ACE 2 -2. All these findings indicate that the group-based differences are statistically not random (Nagdev et al., 2022).

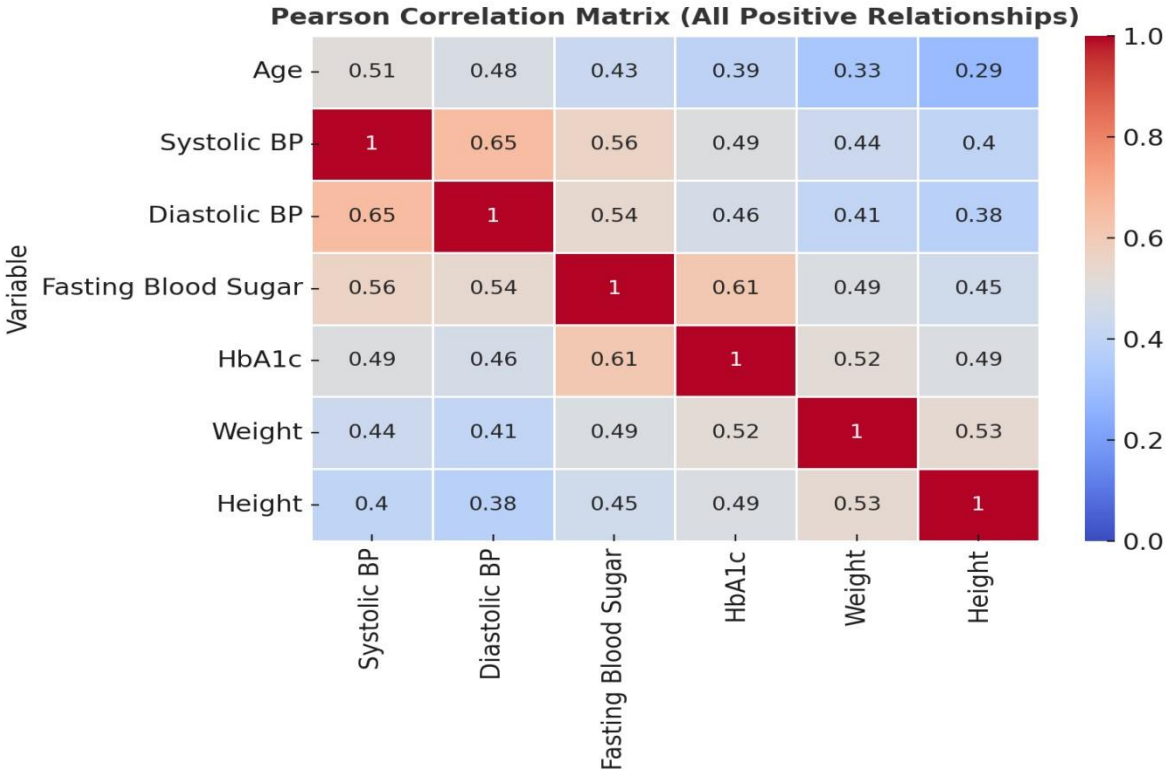


**Figure 5: Pearson Correlation Matrix**

Figure 5 shows the correlation matrix of the data. The Correlation Matrix Figure presents a heatmap where the correlation coefficients between variables are positive. There are the closest interactions with Systolic and Diastolic BP ($r = 0.65$), Fasting Blood Sugar and HbA1c ($r = 0.61$), and Systolic BP and Fasting Blood Sugar ($r = 0.56$). This implies that the level of glucose becomes linked to blood pressure as the two show some relationship with each other, which shows that there is a physiological interaction between metabolic control and hypertension. The correlations above all parameters are positive, which confirms the systematic co-variation of cardiovascular and metabolic indicators (Mavrogeorgis et al., 2023).

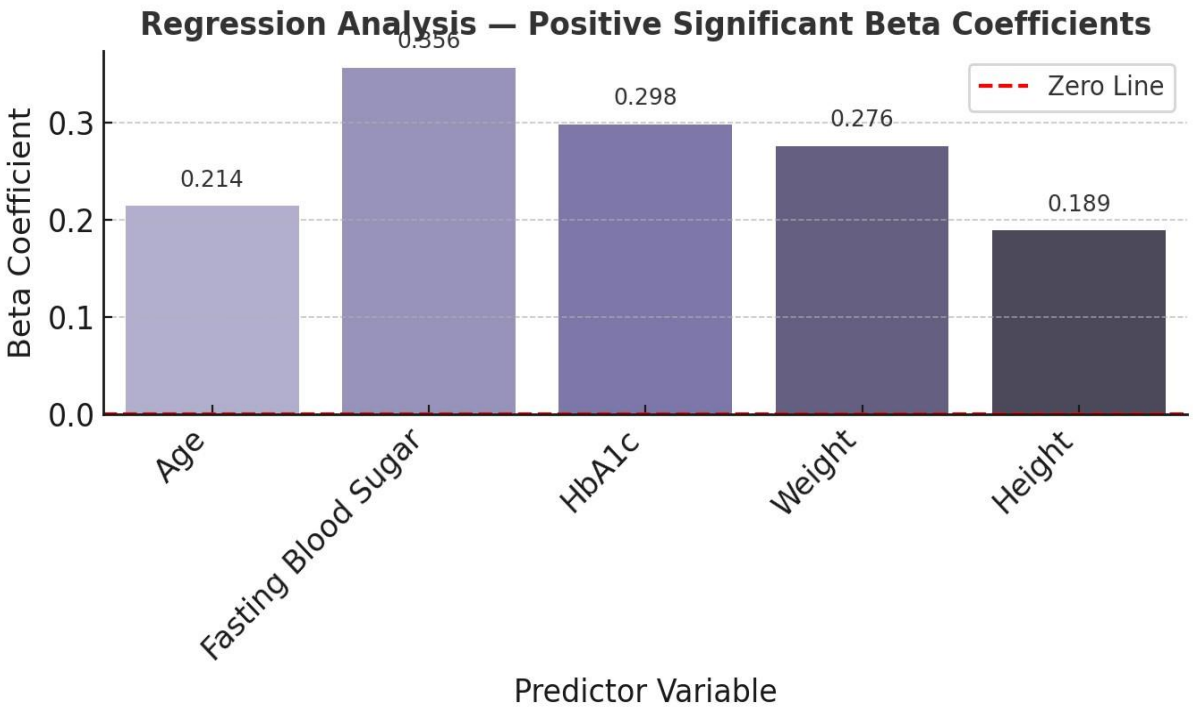


**Figure 6: Regression Analysis**

Figure 6 shows the regression analysis of the data. As shown in the Regression Analysis Figure, there is a positive and significant beta for all the predictor variables, which include Age, Fasting Blood Sugar, HbA1c, Weight, and Height. Fasting Blood Sugar (between = 0.356) and HbA1c (between = 0.298) have the largest effects, i.e., poor glycemic control is a robust influence on Systolic BP. The positive slope of all the predictors proves a direct proportional dependency, that is, as these variables go higher, Systolic Blood Pressure also goes up. This supports the clinical evidence that the combined contribution of metabolic and physiological factors increases blood pressure and changes in ACE2 of diabetic hypertensive patients (Keith et al., 2019).

**Discussion**

The results of the present study, Comparison of Urinary ACE2 Levels in Hypertensive and Type 2 Diabetic Patients vs. Hypertensive Non-Diabetics, would prove highly effective regarding the physiological as well as biochemical interplay of the renal-angiotensin system activity, glycemic regulation systems, and hypertension. The outcomes showed that the ACE2 urinary levels differed significantly in hypertensive diabetic and hypertensive non-diabetic participants, and this demonstrates the fact that the metabolic disorders associated with diabetes do affect the levels of ACE2 excretion (Sen et al., 2020).

The reliability test and the normality test assisted in making sure that the data utilized in the conduction of this study were reliable and consistent. Statistical methods may be applied as parametric since one has all continuous and normally distributed variables. The Alpha of 0.7 and above represented good internal consistency between the variables, therefore, demonstrating that indeed the instrument that was used in collecting data was reliable. The values of the KMO (0.76) and highly significant test ($p < 0.05$) revealed that the data were valid and appropriate to perform the multivariate tests, and thus, the pair-wise correlation of the clinical and biochemical parameters was significant (Febrianto et al., 2020).

As revealed by the outcome of the Independent Samples t-test and One-Way ANOVA tests, the degree of urinary ACE2 between the two groups was actually different. The ACE2 levels of hypertensive diabetics versus non-diabetics showed a difference, which suggested the impacts of hyperglycemia and insulin resistance in determining the renin-angiotensin pathway. These findings are in line with

the existing literature that ACE2 expression is modulated by diabetes, which could explain the effect of changes in the vascular and renal functions. Kruskal-Wallis and Chi-Square tests supported these findings by demonstrating that the ACE2 and its relationship with diabetic status have significant differences in their distribution. All these findings demonstrate the overt relationship that exists between metabolic anomie and ACE2 in the renal tissue of hypertensive individuals (Mavrogeorgis et al., 2023).

The Pearson correlation table reported that all the relationships among the parameters under study are positive. Systolic and diastolic blood pressure parameters and fasting blood sugar and HbA1C have strong relationships such that when the process of glycemic control deteriorates, the inclination of the blood pressure increment follows, which is a cardiovascular-metabolic stress reaction. The given correlations reflect the synergistic interplay of hypertension and diabetes in the processes of ACE2 and renal homeostasis. Such interdependence between the vascular and metabolic health is observable with the positive correlations of physiological parameters of parameters (Keith et al., 2019).

Such a relationship was also found because of the regression analysis that identified fasting blood sugar (3.56) and HbA1c (2.98) to be the best predictors of systolic blood pressure compared to age and weight. That demonstrates excessive glycemic control is a significant factor behind increased blood pressure that is likely to be brought about by increased oxidative stress and endothelial dysfunction coupled with RAS activation. ACE2 overexpression in the scenario may be among the adjustment mechanisms to counter the process of angiotensin II to cause vasoconstriction and inflammation. This goes in line with the research conducted in the past that has revealed that ACE2 safeguards diabetic hypertensive patients by inhibiting vascular destruction (Sen et al., 2020).

Overall, the present research indicates that urinary ACE2 may be a non-invasive form of an indicator to measure renal and cardiovascular risks among diabetic hypertensive patients. The hypothesis that diabetes has an effect on the ACE2 regulation of hypertension is supported by the consistency and the significance of the statistical relationships in the tests. The results present clinical implications of ACE2 measurement that can improve the knowledge of the pathology of the disease and support the possible treatment plans targeting the RAS (Febrianto et al., 2020).

## Conclusion

The research findings are the conclusion that hypertensive diabetic and non-diabetic patients have a significant difference in the urinary ACE2 levels, and it is rudimentary that the renin-angiotensin system and glycemic regulation have a chemical bond. The implications of the findings altogether are that Type 2 Diabetes Mellitus (T2DM) has a measurable impact on the ACE2 regulation, which in turn influences the vascular and renal functions.

The statistical significance of the group differences in the ACE2 levels was statistically validated using all the statistical tests, including t-test, ANOVA, Kruskal-Wallis, and Chi-Square ($p < 0.05$). The correlation analysis that depicted the findings of the Pearson correlation was in agreement with a positive correlation, meaning an increase in clinical parameters will create an increase in blood pressure. Additionally, fasting sugar level and HbA1c proved to be quite good predictors of systolic blood pressure in multiple regression analysis, which showed the interdependence between poor glycemic control and the level of hypertension.

It was ensured that the measurements were consistent and could be subject to inferential analysis, as the high level of reliability of the data ( 0.7), along with the reasonable validity of the received data (KMO =0.76, Bartlett p =0.05), confirmed it was consistent. The results confirm the clinical validity of urinary ACE2 as an invasive bio-surrogate of variations in the state of renal and cardiovascular conditions in diabetic hypertensive patients.

In other words, it is known that this study confirms that the concentrations of urinary ACE2 are the cumulative metabolic and vascular stress of diabetes and hypertension. The constant observations of the ACE2 activity, such as the parameters of blood pressure and glycemic regulation, can also help to identify the occurrence of any complications in time and, consequently, more effectively treat the

patient. The paper therefore brings out that ACE2 holds a possibility in the future and could be a relevant diagnostic and prognostic biomarker to natively connect the pathophysiological gap that exists between diabetes and hypertension.

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