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Association of ketogenic diet with glycemic control and hematological and biochemical parameters in Yemeni patients with primary hypertension.

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Abstract

Introduction: Hypertension is associated with metabolic and hematological alterations that increase cardiovascular risk. Nutritional interventions, such as ketogenic diets, may improve these parameters. This study aimed to evaluate the association between the ketogenic diet and glycemic, hematological, and biochemical markers in patients with primary hypertension over two months.

Method: The repeated-measures study was carried out on 80 diagnosed primary hypertension patients who followed the keto diet program. They were followed during three periods: baseline, before starting the keto diet program, after one month, and after two months of using the keto diet. The results were analyzed using SPSS for statistical analysis.

Results: The results showed that random blood sugar, alanine transaminase, aspartate transaminase, alkaline phosphatase, urea, cholesterol, and triglycerides were significantly decreased (p= $1x10^{-11}$, 0.003, 0.029, 0.0002, 0.0003, $7.2x\ 10^{-13}$, $2.3x\ 10^{-13}$,respectively), but LDL-cholesterol and HDL-cholesterol levels were significantly increased (p= 0.00004, 0.00001, respectively) and hemoglobin, total white blood cell, and platelet count were significantly increased (p= 0.004, 0.073,and 0.023). There were no significant changes in creatinine, Na, K, Mg, Ca, and HbA1C in the hypertensive patients when comparing baseline with one and two months after using the ketogenic diet.

Conclusion: This study concluded that the ketogenic diet positively influenced hematological and biochemical markers without adverse effects on liver or kidney function. These changes collectively suggest that the ketogenic diet may serve as an effective adjunctive strategy for managing hypertension, especially among individuals exhibiting features of metabolic syndrome or insulin resistance.

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1. INTRODUCTION

Hypertension is a major global health problem and a leading risk factor for cardiovascular morbidity and mortality. Patients with primary hypertension frequently present with disturbances in glycemic, biochemical, and hematological parameters, including alterations in lipid metabolism, glucose regulation, and renal or hepatic functions. These abnormalities contribute to cardiovascular risk and highlight the need for interventions to improve systemic physiology [1, 2].

The ketogenic diet, characterized by very low carbohydrate and high fat intake, shifts metabolism from glucose to ketone bodies and has been associated with improved

lipid profiles and glycemic control [3–5]. Despite the growing interest, few studies have comprehensively assessed the impact of ketogenic diets on hematological and biochemical markers in patients with primary hypertension, especially in low-resource settings. In Yemen, adopting such dietary patterns could be pivotal in addressing the growing prevalence of hypertension. However, implementing these dietary changes requires a multifaceted approach, accessibility to healthy foods, and improvements in healthcare infrastructure [6]. This study aimed to evaluate the association between a ketogenic diet and glycemic control, hematological parameters, and biochemical parameters.

MATERIALS AND METHODS

Data Collection and Subjects

A repeated-measures study was conducted at Al-Muayyad Hospital, Yemen, between2024and2025. The study protocol was approved by the Ethics Committee of the Faculty of Medicine and Health Sciences, and informed consent was obtained from all participants. A total of 80 patients diagnosed with primary hypertension were enrolled in the study. Patients with secondary hypertension, pregnancy, or other chronic diseases were excluded. All participants followed a ketogenic diet consisting of high fat, moderate protein, and very low carbohydrate intake. Dietary adherence was monitored using structured questionnaires and clinical follow-ups.

Sample collection

A venous blood sample (8 mL) was obtained from each participant following an overnight fast of over ten hours. The collected blood was immediately transferred into two labelled Vacutainer tubes: the first was a plain tube without any anticoagulants used for biochemical assays, and the second tube containing K2EDTA used for CBC count and glycated hemoglobin (HbA1c). For biochemical analysis, the serum from each sample was separated within 30 minutes, aliquoted into Eppendorf tubes, and promptly stored at -20°C

Hematological and Biochemical Analyses

Hemoglobin (Hb), total white blood cell (WBC), platelet, blood glucose, HbA1c, FBS, creatinine, urea, liver function, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), blood electrolyte Na, K, Ca, Mg, lipid profile, total cholesterol, triglycerides, high-density lipoprotein (HDLc), and low-density lipoprotein (LDLc) levels were measured using Cobas c 501analyzers (Roch, Germany).

Statistical Analysis

The results were analyzed using the Statistical Package for Social Sciences (SPSS) software version 21 (IBM Inc., New York, USA). Mean $\pm$ SD was used for normally distributed data, and geometric mean (95 % confidence interval for mean) was used for transformed data after using rank-based inverse normal transformation. Repeated measures ANOVA: One-way was used to assess the significant difference in the same group. Equations for blood sugar and HbA1c were formulated using simple linear regression.

Results

The results in Table 1 show that random blood sugar, alanine transaminase, aspartate transaminase, alkaline phosphatase, urea, cholesterol, and triglycerides were significantly decreased (p= 1 × 10 $^{-11}$,0.003, 0.029, 0.0002, 0.0003, 7.2 × 10^{-13}, 2.3 × 10^{-13},respectively), although LDL-cholesterol and HDL-cholesterol levels were significantly increased (p= 0.00004, 0.00001, respectively), and hemoglobin, total white blood cells, and platelet counts were significantly increased (p= 0.004, 0.073, 0.023, respectively). There were no significant changes in creatinine, Na, K, Mg, Ca, and HbA1c levels in Yemeni hypertensive patients when comparing baseline with one and two months after following the ketogenic diet.

Table 2 shows the variables used to estimate the simple linear regression equation to predict the values of HbA1c, [HbA1c is the dependent variable (Y)], and can be predicted from blood sugar [independent variable (X)], so the equation derived from linear regression:

$$[Y = 3.4 + 0.018X].$$

$$HbA1c(Y) = Constant + B\ x\ Blood\ sugar(X)$$

$$HbA1c(\%) = 3.4 + 0.018\ x\ blood\ sugar$$

According to Table 2, the result shows that HbA1c level increases by 0.018% for every one mg/dL increase in blood sugar (b= 0.018, p= 1.2x10^{-40}).

DISCUSSION

This study investigated the short-term effects of a ketogenic diet on glycemic, biochemical, and hematological parameters in Yemeni patients with primary hypertension and revealed significant improvements in blood pressure, fasting blood sugar, liver enzymes, and lipid profile, while renal function and electrolytes remained stable. Fasting blood sugar showed a significant decrease, indicating an early metabolic benefit of carbohydrate restriction, whereas HbA1c did not change significantly, which may

Table 1. Biochemical and hematological tests in Yemeni hypertensive patients using the ketogenic diet.

Variable	Base line	After one month	After two months	P - value
FBS mg/dl	129(114.6-143.3)	113.3(102.5-124)	102.7(93.8-111.7)	$1x10^{-11}$
HbA1c %	5.69(5.4-5.9)	5.68(5.4-5.9)	5.59(5.3-5.8)	0.138
ALT(U/L)	22.6 ± 7.6	19.8 ± 6.5	18.8 ± 5.7	0.003
AST(U/L)	22.3(20 – 24.7)	22.8 (21.5 – 24.1)	20.5 (19.5 -21.5)	0.029
ALP(U/L)	84.8 ± 24.1	88.3 ± 22	76.7 ± 15.8	0.0002
urea(mg/dl)	22.8(21.4 – 24.2)	20.2(19 -21.4)	18.7(17.4 – 20)	0.0003
Creatinine (mg/dl)	0.76(0.70-0.82)	0.75(0.71-0.85)	0.71(0.66 -0.75)	0.262
Cholesterol (mg/dl)	140.4(128.5-152.3)	134.6(123-146.3)	135.8(124.7-146.9)	$7.2X0^{-13}$
TG (mg/dl)	154.2(141-167.2)	148.2(135.4 – 161)	145.4(133.5-157.3)	$2.3X10^{-13}$
HDL (mg/dl)	53.3 ± 14.7	50.5 ±12.5	56.5 ±13	0.00001
LDL (mg/dl)	52.2(47.5 – 56.8)	54.2(49.9-58.6)	56.2(52.4-59.9)	0.00004
Mg (mg/dl)	1.69(1.60-1.78)	1.44(1.35-1.52)	1.77(1.69-1.85)	0.715
Na (mmol/L)	139.1(138.4-139.9)	138.6(138.1 – 139.1)	139.7(139.3-140.1)	0.564
K (mmol/L)	4.04(3.95-4.15)	4.0(3.93-4.08)	3.99(3.91-4.06)	0.602
Ca (mg/dl)	9.16(9.0- 9.28)	9.14 (9.0 – 9.23)	9.20(9.15 – 9.26)	0.139
Hb (g/dl)	13.33±1.35	13.31±1.23	13.51±1.15	0.004
WBC (10^9/L)	4.8(4.6-5.1)	5.0(4.9-5.1)	5.1(5.0-5.3)	0.073
PLT (10^9/L)	225 (212.6-238.8)	233 (224.5-241.3)	239.8 (232.7-246.8)	0.023

Data presented as geometric means with 95% confidence interval of the mean for all parameters except for ALT, ALP, HDL-c, LDL-c, and HbA1c presented as Mean $\pm$ SD. P-value significant at ≤ 0.05.

be explained by the short duration of the study, as HbA1c reflects average glycemic control over three months [3]. The regression analysis further demonstrated a strong linear relationship between random blood sugar and HbA1c, with an R^2 value of 0.601, indicating that approximately 60% of the variability in HbA1c could be explained by changes in random blood sugar. The derived equation (HbA1c =3.4+0.018$\times$ RBS) confirmed that each 1 mg/dL increase in blood sugar corresponds to an increase of0.018% in HbA1c, while the reciprocal equation (RBS =32.7$\times$ HbA1c $-$ 60.8) demonstrated that blood sugar can also be predicted from HbA1c. These findings highlight the close correlation between the two parameters and provide additional clinical value, particularly in short-term interventions, where HbA1c may not change significantly, but random blood sugar can serve as a sensitive early indicator of metabolic improvement. This observation is in line with earlier reports that confirmed a strong correlation between HbA1c and plasma glucose levels and emphasized the clinical utility of regression models in predicting glycemic status [4–6].

The significant decline in liver enzymes, such as ALT, AST, and ALP, suggests an improvement in hepatic function, in agreement with studies reporting reduced hepatic steatosis and improved liver metabolism with ketogenic diets [7]. Renal function markers, including creatinine and urea, showed no significant variation, confirming that the diet did not adversely affect kidney function, which aligns with reports that ketogenic diets are safe for individuals without pre-existing renal diseases [8]. With respect to the lipid profile, the decrease in total cholesterol and triglyceride levels, along with the increase in HDL cholesterol, represent favorable changes that are consistent with previous studies [9]. However, the slight increase in LDL cholesterol requires cautious interpretation, as some evidence indicates that this may be a transient effect or associated with a shift toward larger, less atherogenic LDL particles; however, longer-term studies are needed to clarify the clinical implications [10]. Hematological results showed significant increases in hemoglobin and platelet levels within the normal range, which may reflect improved nutritional and metabolic bal-

Table 2. Variables used to estimate the simple Linear Regression Equation to predict values of HbA1c from Random blood sugar.

	B	R square	F	p- value
Blood sugar	0.018	0.601*	297.7	2.5×10^{-41}
Constant	3.4			5×10^{-61}

Constant 3.4 5 x10-61 * This value interprets 60.1% of the relationship between HbA1c and random blood sugar, and the rest of the percentage (39.9%) may be explained by other factors.

ance, whereas white blood cell counts remained stable, suggesting no inflammatory response. These findings are in line with those of earlier studies demonstrating that ketogenic diets may reduce low-grade inflammation and improve hematological balance [11]. Electrolyte levels, including sodium, potassium, calcium, and magnesium, did not show significant changes, which is important because electrolyte disturbances are often a concern during ketogenic diets, and the observed stability may reflect the value of dietary counseling and close follow-up [12]. Taken together, the results of this study suggest that the ketogenic diet may serve as a safe and beneficial adjunctive strategy for managing primary hypertension in Yemen, where healthcare resources are limited, and dietary approaches can represent cost-effective and culturally adaptable solutions.

LIMITATIONS

This study has some limitations, including its relatively short follow-up period, which did not allow long-term evaluation of HbA1c or cardiovascular outcomes, and the absence of a randomized control group that limits causal inference.

CONCLUSION

Adherence to a ketogenic diet for two months positively affected hematological and biochemical markers in patients with primary hypertension, without adverse effects on liver or kidney function, suggesting it is a safe and effective dietary intervention.

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