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Evaluation of Serum Electrolytes Disturbances among Type 2 Diabetes Mellitus Patients in Dhamar, Yemen.

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Abstract:

Background: Diabetes is one of the diseases which frequently lead to electrolyte distortion. Aim: This study was conducted to evaluate the electrolytes disturbances and associated risk factors in type 2 diabetes mellitus patients. Methodology: A Case-control study was conducted on 70 type 2 diabetes mellitus patients and 70 apparently healthy persons in Dhamar city. Data were collected using questionnaires, sociodemographic and clinical data were reported through direct interview. Anthropometric measurements were estimated in the hospital during interview. Blood samples for estimation of glucose and electrolytes were collected from all participants after overnight fasting state. Laboratory measurement for glucose, sodium, potassium, calcium and magnesium were carried out using commercial kits. Data were analysis using SPSS and p value of <0.05 was assumed significant **Results**: In this study, the control group had 34% males and 65.7% women, while the diabetes group included 68.9% men. Diabetics had higher serum potassium and calcium levels, with a higher prevalence of hypernatremia (18.9% vs. 1.4%), hyperkalaemia (41.9% vs. 2.9%), and hypermagnesemia (9.5% vs. 2.9%) compared to controls. The

study found that patients with FBS levels above 130 mg/dl, patients over 40 years of age, male subjects and hypertensive patients had significantly higher serum potassium levels. Patients with FBS values over 130 mg/dl and patients with high blood pressure also had significantly higher sodium concentrations. Increased age is positively correlated with FBS and potassium levels, while magnesium and BMI show negative correlations. There are positive correlations between magnesium, calcium and potassium. **Conclusion:** Diabetic patients have a higher prevalence of electrolyte imbalance, possibly due to glucose homeostasis dysregulation. Future research is needed to establish a reference interval for electrolytes in adult Yemeni populations.

Keywords: Yemeni, Diabetics, Electrolyte imbalances

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Introduction:

Diabetes has become increasingly prevalent worldwide and is now recognized as one of the most widespread noncommunicable diseases. According to the latest edition of the IDF Diabetes Atlas for the year 2021, an alarming 10.5% of adults aged between 20 and 79 years worldwide are currently grappling with diabetes. What's more concerning is that nearly half of these individuals are oblivious to their diabetic status, living with the condition unknowingly (1).

Numerous studies and investigations have consistently highlighted the alarming fact that diabetes is a leading cause of a variety of serious health complications including blindness, kidney failure, heart attacks, stroke and the unfortunate need for lower limb amputation (2,3).

Electrolytes are crucial for maintaining normal cell function and conducting nerve and muscle activity. Important electrolytes include sodium, potassium, chloride. magnesium, calcium. phosphate, and bicarbonates (4). Diabetes can cause metabolic imbalance and disruptions in electrolyte concentration, which can have a significant impact on the body. The cause is usually multifactorial, but usually results from insulin deficiency or insulin resistance, diabetic ketoacidosis and hyperglycaemias (5). The mechanism of electrolytes changes involves osmotic effect of hyperglycaemias, distribution of water movement between intra and extracellular compartments, and the activity of Na+/K+ ATPase pump. Insufficient insulin production or insulin resistance can lead to reduced activity of a transporter protein that maintains the balance of sodium and potassium concentration. This can result in changes in electrical gradients and further affect electrolytes levels (5,6). The most common pattern of electrolytes disturbances in diabetic patients are, hyponatremia, hypomagnesemia, hypocalcaemia,

and dyskalaemia (7). Hyperkalaemia is more common in diabetic patients compared to the general population (7,8). This can occur when potassium moves from inside the cells to the outside, causing an increase in potassium levels without an overall increase in the body's total Acidosis, potassium. insulin deficiency, hypertonicity, cell breakdown, and certain medications like beta blockers can all contribute to this type of hyperkalaemia in diabetes (6,8). On the other hands hypokalaemia in diabetics was reported in several studies (7,10) which could be attributed to shift hypokalaemia due to insulin administration, renal loss of potassium ions due to osmotic diuresis, Hypomagnesemia which lead to activates the renal outer medullary potassium ions channel to secrete more potassium ions (10).

Since the electrolytes play a crucial role in maintaining normal physiological function. Imbalances in these electrolytes can have neurological and cardiac effects such as seizures and abnormal heart rhythms. Bicarbonate imbalance can also lead to metabolic acidosis or alkalosis. In diabetics, these predictions should not be taken lightly as they highlight the urgent need for increased awareness, prevention and of electrolyte treatment imbalances. Furthermore, like others in Yemen, diabetics suffer from lack of health care, economic problems and poor education, making it impossible for them to properly assess their clinical situation on a regular basis. In addition, there is very limited research on this topic in diabetics. Therefore, this study aimed to evaluate the electrolyte imbalances in diabetics.

MATERIALS AND METHODS

Study design and population:

A Case-control study was conducted on 70 type 2 diabetes mellitus patients and 70 apparently healthy persons attending Dahmar General Hospital Commission in Dhamar city. The sample size was calculated based on the power (1-beta) = 0.8, the ratio of the sample size, control/case = 1, the event probability in the case group = 0.83 and the event probability in the control group = 0.52 over the previous determined study and 2-sided significance level = 0.05 (11). The sample size was 41 for the control group and 41 for the case group. Because the estimate was for overall electrolyte imbalance and the variability was high for certain electrolytes, we increased the sample size to 70 for both groups.

Data were collected using questionnaires, and sociodemographic and clinical data were reported through face-to-face interviews. During the interview, anthropometric measurements and physical examinations were performed in the hospital. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the right arm after 15 minutes of rest in a sitting position.

Laboratory tests:

Venous blood samples were taken from all subjects after an 8-12-hour overnight fast and transported to the laboratory for testing. Serum levels of glucose and electrolytes, including sodium, potassium, calcium and magnesium, were estimated spectrophotometrically using commercially available kits.

Parameters definition:

The electrolyte imbalances were defined based on the reference intervals for each electrolyte as follows: sodium (135–145 mmol/l), potassium (3.5–5.0 mmol/l), magnesium (1.7–2.8 mg/dL), and calcium (8.0–10.4 mg/dl). Values above or below these ranges for each individual electrolyte were considered hypo or hyper. FBS was defined as a poor control at a level of 130 mg/dl (16). BMI was classified as overweight or obese (BMI 25.0 kg/m2) and not overweight (BMI <25.0 kg/m2) (37). Hypertension is defined as a systolic blood pressure (SBP) of 140 mm Hg, diastolic blood pressure (DBP) of 90 mm Hg, or self-reported use of antihypertensive medication (16).

Data analysis:

The data were analysed with SPSS 22. Categorical data were presented as frequency and percentage. FBS and electrolyte values were expressed as mean with standard deviation. The t-test was used to compare the mean of FBS and electrolytes in controls and diabetics. A correlation study was conducted between electrolytes and glucose, BMI and age. p-values less than or equal to 0.05 were considered statistically significant.

RESULTS

General characteristics of the study population

The characteristics of the study population are presented in Table 3:1. In this study, most of the diabetic participants were over the age of 40. The distribution of gender between the control and diabetic groups was 34% male, 65.7% female for the control group and 68.9% male, 31.1% female for the diabetic group. Approximately 64.9% of the diabetics had a BMI higher than 25 kg/m2, compared to 35.1% in the control group. The majority of participants in this study were unemployed. Around half of the study population had a family history of diabetes. More than twothirds of the diabetics followed a diet, while only 1.4% of the control subjects were on a diet.

Parameters		Control subject	Diabetic subjects
Age year	>40	10 (14.3%)	65 (87.8%)
	≤40	60(85.7%)	9 (12.2%)
BMI kg/m2	<25	50 (71.4%)	20 (28.6%)
	≥25	26 (35.1%)	48 (64.9%
Sex	М	24 (34.3%)	51(68.9%)
	F	46(65.7%)	32 (31.1%)
Occupation	Employed	22 (31.4%)	25 (33.8%)
	Unemployed	48(68.6%)	49 (66.2%)
Family history	Yes	34 (48.6%)	43 (58.9%)
of T2DM	No	36 (51.4%)	30 (41.1%)
Hypertension	Yes	2 (2.9%)	34 (45.9%)
	No	68 (97.1%)	40 (54.1%)
Kidney	yes	32 (45.7%)	52 (70.3%)
	No	38 (54.3%)	22 (29.7%)
Eye	Yes	2 (2.9%)	30 (40.5%)
	No	68 (97.1%)	44 (59.5%)
Diet	No	69 (98.6%)	23 (31.1%)
	Yes	1 (1.4%)	51 (68.9%)

Table 1. General characteristics of the study population

Levels of glucose and electrolytes in diabetic and control subjects

The differences of FBS and electrolytes mean levels in diabetic patients and control were shown in table 2. The result indicated that FBS, serum potassium, and calcium levels in diabetic patients were significantly higher than control (p <0.05). Serum sodium and magnesium levels were also slightly increased in diabetic patients compare to control, but without statistical significances.

 Table 2. Levels of glucose and electrolytes in diabetic and control subjects

Parameters	Subjects	Ν	Mean	Std. Deviation	P value
FBS mg/dl	Diabetes	74	193.70	74.87	0.000
	Control	70	97.41	11.21	
K mmol/l	Diabetes	74	4.70	0.780	0.000
	control	70	4.10	0.49	
Na mmol/l	Diabetes	74	137.20	10.62	0.153
	control	70	135.10	5.90	
Mg Mg/dl	Diabetes	74	1.70	0.44	0.254
	control	70	1.60	0.29	
Ca mg/dl	Diabetes	74	8.6	1.00	0.044
	control	70	8.30	0.88	

Serum Levels of FBS and electrolytes based on population characteristics

The levels of FBS and electrolytes based on populations characters are shown in table 3. FBS was found to be high in male patients, subject with age over 40 years, patient had no diet adherence, and hypertensive patients. The result of this study also indicated that High sodium concentration found in patient with FBS over 130 mg/dl (P 0.002) and patient with hyper tension (P 0.064). According to gender, age over 40 years

and BMI over 25 kg/m2 concentration of sodium was not significantly differed. On the other hand, serum potassium was significantly higher in male (P 0.002), age over 40 years (P 0.000), patients with FBS more than 130 mg/dl (P 0.001), hypertensive patients (P 0.000) and in subjects who had no diet (P 0.000), While the serum calcium and magnesium were not significantly changing according to the categories of age, BMI, FBS and hypertension, significant differences in the levels of calcium was found between male and female (p 0.006).

Characters	Category	No	Mean ± Standard deviation				
			FBS	Na+	K +	Mg++	Ca++
			mg/dl	mmol/l	mmol/l	mg/dl	mg/dl
Gender	М	75	165.74 ± 78.54	136.94 ± 8.86	4.60 ± 0.73	1.72 ± 0.42	8.70 ± 0.94
	F	69	126.41 ± 59.32	135.40 ± 8.50	4.21 ± 0.66	1.63 ± 0.36	8.21 ± 0.92
	Р		0.001	0.289	0.002	0.184	0.006
Age	>40	75	182.70 ± 78.52	136.70 ± 10.70	4.63 ± 0.80	1.70 ± 0.42	8.5 ± 1.0
	≤40	69	108.01 ± 37.33	135.70 ± 5.70	4.20 ± 0.52	1.70 ±0.33	8.4±0.90
	р		0.000	0.475	0.000	0.690	0.693
BMI kg/m2	≥25	68	153.60 ± 63.60	135.60 ± 9.22	4.34 ± 0.75	1.61 ± 0.41	8.50 ± 1.04
_	<25	76	140.92 ± 79.60	136.80 ± 8.20	4.50 ± 0.69	1.73 ± 0.33	8.40 ± 0.88
	р		0.297	0.420	0.343	0.050	0.644
FBS mg/dl	≥130	38	215.45 ± 68.05	138.19 ± 10.52	4.64 ± 0.80	1.73 ± 0.46	8.60 ± 1.2
	<130	106	99.31 ± 12.26	134.83 ± 6.88	4.23 ± 0.64	1.64 ± 0.31	8.40 ± 0.94
	р		0.000	0.002	0.001	0.177	0.207
Hypertension	Yes	36	167.90 ± 64.42	138.52 ± 10.60	4.82 ± 0.80	1.64 ± 0.41	8.60 ± 1.12
	No	108	139.90 ± 73.94	135.43 ± 7.90	4.30 ± 0.64	1.70 ± 0.37	8.40 ± 0.89
	Р		0.045	0.064	0.000	0.534	0.245
Diet	No	69	182.66 ± 78.53	136.71 ± 10.73	4.60 ± 0.80	1.69 ± 0.42	8.50±1.0
	Yes	75	108.01 ± 37.33	135.66 ± 5.73	4.20 ± 0.53	1.66±0.33	8.40±0.90
	P		0.000	0.470	0.000	0.690	0.693

Frequencies of abnormal levels of electrolytes among diabetics and control subjects

The frequencies of abnormal levels of sodium, potassium, magnesium and calcium are shown in table 4. The result indicated that patients with diabetes mellitus had higher frequencies of abnormal high levels of sodium (18.9%) potassium (41.9%), magnesium (9.5%) than control. Abnormal high levels of magnesium and calcium were also found in diabetic patients more than control. Normal levels of sodium and potassium were found in 40.5% and 50 % of diabetic patients which is lower that of the control 58.6% and 88.6%. The distribution of low levels of sodium, potassium, magnesium, and calcium in diabetic patients were found to be not much different from those in the control.

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Parameters		Diabetic patients	Control
		Frequencies (%)	Frequencies (%)
Na	Normal	30 (40.5%)	41(58.6%)
	High	14 (18.9%)	1 (1.4%)
	Low	30 (40.5%)	28 (40 %)
K	Normal	37 (50 %)	62 (88.6%)
	High	31(41.9%)	2 (2.9%)
	Low	6 (8.1%)	6 (8.6%)
Mg	Normal	29 (39.2%)	29 (41.4%)
	High	7 (9.5%)	2(2.9%)
	Low	38 (51.4%)	39 (55.7%)
Ca	low	21 (28.4%)	26 (37.1%)
	Normal	51 (68.9%)	44 (62.9%)
	High	2 (2.7%)	0 (0.0%)

Table 4: Frequencies of abnormal levels of electrolytes among diabetics and control subjects

Correlation of age, BMI, FBS and electrolytes

Correlation analysis (table:5) revealed that increased age was positively correlated with levels of FBS (r= 0.561^{**}) and potassium (r= 0.322^{**}). Increased levels of FBS were correlated with higher serum potassium concentration (r= 0.318^{**}). We found no significant correlation between levels of FBS and sodium, calcium, and magnesium. Magnesium and BMI was found to be negatively correlated while there was positive correlation between magnesium with calcium ($r=0.265^{**}$) and potassium (r=0.162). There was a positive correlation between potassium and calcium ($r=0.294^{**}$). No correlation was found between sodium with magnesium, and calcium.

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Parameter	Pearson Correlation (r)	Significance		
Age & FBS	0.561**	0.000		
AGE & K	0.322**	0.000		
BMI & mg++	-0.224**	0.007		
FBS & Na	0.141	0.092		
FBS & K	0.318**	0.000		
FBS & Ca	0.135	0.106		
FBS & Mg	0.061	0.466		
Na & K	0.090	0.248		
K & Ca	0.294**	0.000		
Na & Mg	0.040	0.617		
Mg &Ca	0.265**	0.001		
Mg & K	0.162	0.052		
**. Correlation is significant at the 0.01 level (2-tailed).				

DISCUSSION

Diabetics are more prone to developing electrolyte imbalance (ED) due to various mechanisms including hyperglycaemia-induced osmotic fluid shifts or by osmotic diuresis, cell shifts from intracellular to extracellular space, from extracellular to intracellular space, caused by insulin deficiency or insulin administration, diabetic ketoacidosis. Metabolic acidosis and associated diabetic chronic kidney disease (5,6,7). The main purpose of the work was to draw attention to the electrolyte imbalances in type 2 diabetes mellitus in the city of Dhamar.

Our results describe the concentration of electrolytes both in the control group and in the diabetic group (Table 3.2). Diabetics had significantly higher serum potassium and calcium levels compared to controls (p<0.05). Conversely, diabetics also had slightly elevated serum sodium and magnesium levels compared to controls, but these differences were not statistically significant. The occurrence of diabetes and hyperkalaemia is a well-known phenomenon. The most likely explanation for hyperkalaemia in diabetes is increased potassium release from cells due to intracellular dehydration (12), insulin deficiency leading to inhibition of Na+-K+-ATPase pump function, and decreased maintenance of the intracellular K+ gradient - and extracellular environments (13). In addition, administration of certain medications, such as angiotensin-converting enzyme inhibitors, can decrease potassium secretion from the kidney (14). Hypercalcemia in diabetes has been reported to be associated with dehydration, insulin resistance leading to hyperparathyroidism, inhibition of insulin growth factor 1 by hyperglycaemia, and decreased bone mineralization (15).

Our results indicated an electrolyte abnormality in the diabetic and control groups (Table 3.4). The most common electrolyte disturbances were hyperkalaemia (41.9% vs. 2.9%), hyponatremia (40.5% vs. 40%), hypernatremia (18.9% vs. 1.4%), hypomagnesemia (51.4% vs. 55.7%), hypermagnesemia (9.5% vs. 2.9%). and hypocalcaemia (28.4% VS. 37.1%). The prevalence of hyperkalaemia in our study was higher than in patients enrolled in Ethiopia (9.2%) (16) and southern India (6%) (17). One of the mechanisms of hyperkalaemia is cellular dehydration due to hyperglycaemia, which leads to increased intracellular K+ concentration and favors a gradient for the transport of K+ out of cells. Diabetic nephropathy and hyporeninaemic hypoaldosteronism are commonly observed in people with diabetes (15,18,19,), resulting in decreased glomerular filtration and tubular potassium secretion (15). On the other hand, 8.1% of diabetics were found to have hypokalaemia, consistent with the prevalence of hypokalaemia reported in Thailand (6.7%) and lower than in Ethiopia (22.3%) and India (16,17,20). The disparity may be due to the diversity of target groups or related to the severity of DM cases. However, this study found that there is no significant difference between the hypokalaemia of diabetic patients and the hypokalaemia of controls. Some factors associated with hypokalaemia in diabetics, such as B. the potassium shift due to insulin potassium loss via administration, the gastrointestinal system, osmotic diuresis and low magnesium levels have also been reported (15).

Hyponatremia in this study (40.5%) was comparable with other studies which carried out in Ethiopia and India which have shown that prevalence of hyponatremia among diabetic patients were 39.2% [95% CI: 31.1-47.9] and 33% respectively (16, 17). Compared to the control group, the frequency of hypernatremia (18.9% vs. 1.4%) was high in our study. Several previous studies reported that the prevalence of hypernatremia in diabetics ranges from 11.4% to 17.3% (16,21,22). The increase in hypernatremia prevalence may be due to the fact that diabetics are more likely to have hyperlipidaemia, which is suspected to reduce plasma water and cause pseudohypernatremia (15). Additionally, some literature reports have found that impaired glucose metabolism due to insulin deficiency and glucagon-induced gluconeogenesis was associated with hypernatremia and hyperosmolarity in human and animal models (15). It is known that hyperglycaemia can change sodium levels in the opposite direction. Therefore, hypernatremia and hyperosmolarity

should be considered as contributing factors to the occurrence of hyperglycaemia in critically ill patients (23).

Previous research has documented that hypomagnesemia is a common electrolyte abnormality in diabetics (15) and that subjects 55 and older have a high odd of developing hypomagnesemia (OR = 3.32; 95% CI: 2.00-5 .50) (23).In the general population. hypomagnesaemia has been shown to range from 2.5% to 15%, and the prevalence is even higher in critically ill patients, estimated at 65% in one study (25). There are several theories that explain why diabetics often have low levels of magnesium in their bodies. These theories include kidney loss, loss via the gastrointestinal tract, poor diet, excessive filtration in the kidneys, changes in insulin metabolism, use of diuretics, and recurrent metabolic acidosis. It is believed that the main cause of hypomagnesemia in diabetics is osmotic diuresis, which leads to excessive loss of magnesium through the urine (15). Magnesium deficiency has been reported to promote inflammation by disrupting immune function by stimulating phagocytes, increasing oxidative granulocyte burst. activating endothelial cells, and increasing cytokine levels (26). In addition, epidemiological data indicate that patients with serum hypomagnesemia are at increased risk for cardiovascular disease, T2DM, and mortality from these diseases (27).

prevalence of The increased electrolyte imbalances in diabetics and controls, on the other hand, could be due to multifactorial reasons, including geographic characteristics, dietary habits, and food and vegetable availability. In Yemen, it is customary to chew a green leaf called khat. Khat belongs to the Celastraceae family and contains the compounds cathinone and cathine, which are similar to amphetamines. It is believed to be a naturally occurring stimulant derived from the Catha edulis plant and is commonly consumed in Yemen and East African countries (28). An animal study by Limenie et al. (2022) performed on male Swiss albino rats given raw khat extract at doses of 100 mg/kg, 200 mg/kg and 300 mg/kg for 12 weeks found a significant decrease in sodium and calcium concentrations. The K+ concentration was significantly increased in rats receiving raw khat extract 300 mg/kg compared to the control group and in rats receiving raw khat extract 100 mg/kg. Potassium has been found to increase in serum potassium (29).

This study also showed a high prevalence of hypocalcaemia in the diabetic and control groups (28.4% vs. 37.1%). The cut-off we used to define hypocalcaemia in this study was 8.0 mg/dL and hypercalcemia was 10.2 mg/dL. Several factors regulate calcium levels in our bodies, including parathyroid hormone (PTH) and 1,25dihydroxyvitamin D (1,25[OH]2D) in the kidneys, bones, and gastrointestinal tract (30). So far it has been reported that 18% of all hospitalized patients and 85% of patients in the ICU suffer from hypocalcaemia (31). The prevalence of hypocalcaemia in our study was higher than that reported by Eshetu et al. reported. (15.3%) (15) and lower than Cameron (48%) (33). In contrast, the hypercalcemia in our study (2.7%) was consistent with previous data reporting that the prevalence of hypercalcaemia in hospitalized patients was 2.4% (34) and lower than that reported by Catalano et al., who determined the prevalence of hypercalcaemia 4.74% (35).

According to our results, older age and FBS were positively associated with serum potassium (Table 3.5). This could be related to cellular dehydration caused by hyperglycaemia, insulin deficiency and diabetic nephropathy in the elderly. The negative correlation between BMI and serum magnesium found in our study is consistent with previous findings that hypomagnesemia was associated with a five-fold increased risk of metabolic syndrome and that magnesium levels were negatively correlated with waist circumference and BMI (36). The

positive correlation between calcium and potassium levels is partially related to hyperglycaemia, cellular dehydration, metabolic acidosis, and insulin resistance (15). In this study, the serum level of magnesium showed a significant positive correlation with the serum calcium level. This association is attributed to magnesium's metabolic role in regulating parathyroid hormone secretion. In addition, low serum Mg2+ levels can secondarily trigger hypokalaemia, hypocalcaemia, and hypophosphatemia, which may be further related to the long-term complications of DM (15).

Although this study provides innovative information on electrolyte imbalances, the analysis does not allow us to determine the cause of electrolyte imbalances in patients and controls. Some other electrolytes such as chloride and phosphorus were not considered in this study.

Conclusion: Diabetic individuals had a much greater prevalence of electrolyte abnormalities. According to this study, electrolyte imbalance in diabetes patients may be caused by disruption of glucose homeostasis. The high prevalence of low electrolytes levels in healthy participants **References**

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highlights the need for more study to develop an adult Yemeni population electrolyte reference interval that is really future-proof.

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Author Contributions:

Abdulqawi A. A. and Abdulrahman A. and designed the study. The remaining authors participated in data collection, sampling and conducting the laboratory experiments. Abdulqawi A.A. took the lead in writing the manuscript. Abdulrahman A. contributed to the discussion and interpretation of the results. All authors reviewed the results and approved the final version of the manuscript.

Conflicts of Interest:

All authors declare no conflicts of interest.

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