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ORIGINAL ARTICLE

Prevalence and Clinical Implications of Electrolyte and Mineral Imbalances in Diabetic and Non-Diabetic Individuals: A Multicenter Cross-Sectional Study in Pakistan

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ABSTRACT
Background: Electrolyte and mineral imbalances are frequently observed in individuals with diabetes mellitus and are associated with systemic complications, including cardiovascular and renal risks. Despite their clinical significance, such imbalances remain underexplored in the local population.
Aim: To evaluate the levels of serum electrolytes (Na^+, K^+, Cl^-) and minerals (Ca^{2+}, Mg^{2+}) in diabetic and non-diabetic individuals and to investigate their correlation with glycemic control and disease progression.
Method: A cross-sectional study was conducted involving 300 participants (150 diabetics, 150 non-diabetics) aged 30-70 years. Serum electrolyte and mineral levels were measured using ion-selective electrodes and spectrophotometry. Glycemic control was assessed via HbA1c levels. Statistical analyses were performed to identify significant differences and correlations.
Results: Diabetic individuals showed significantly lower levels of Na^+, Ca^{2+}, and Mg^{2+} and higher levels of K^+ and Cl^- compared to non-diabetics. Poor glycemic control (HbA1c > 8%) was strongly linked to hypomagnesemia (47%) and hypocalcaemia (38%), highlighting the impact of uncontrolled diabetes on electrolyte balance.
Conclusion: Electrolyte and mineral imbalances are prevalent in diabetic individuals, especially those with poor glycemic control. Regular monitoring and targeted interventions are essential to mitigate associated complications and improve overall diabetes management.
Keywords: Diabetes mellitus, electrolyte imbalance, glycemic control, serum magnesium, hypocalcaemia, metabolic monitoring.

INTRODUCTION
Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia because of defects in insulin secretion, insulin action, or both. Due to its rising prevalence, DM is being recognized as a global health problem, particularly affecting low- and middle-income countries[1]. Pakistan, along with Afghanistan, is ranked among the top ten countries with the highest diabetes burden, and the diabetes prevalence in Pakistan has shown an alarming rise to over 19 percent among adults. This is a combination of genetic predisposition, urbanization, dietary and sedentary lifestyles that accounts for the increasingly steep incidence. Sodium (Na+), potassium (K+), chloride (Cl-), calcium (Ca2+) and magnesium (Mg2+) are all important electrolytes that play a crucial role in maintaining physiological homeostasis, including nerve conduction, muscle contraction, and enzymatic activities[2]. Chronic hyperglycemia in diabetic patients leads to osmotic diuresis and alterations of renal function, with marked disturbances of electrolyte and mineral balance. These imbalances can further complicate the development of cardiovascular diseases, neuropathy and nephropathy that are common in diabetic populations[3].

Electrolyte disturbances' pathophysiology in DM is multifactorial. The hyperglycemia induces osmotic shifts, which in turn cause dilutional hyponatremia, and insulin resistance affects the Na+/K+ ATPase pump, resulting in intracellular potassium depletion[4]. Additionally, chronic hyperglycemia decreases renal reabsorption of magnesium and calcium resulting in their depletion. Specifically, hypomagnesemia is associated with worsening of insulin resistance and poor glycemic control, leading to a vicious cycle that makes diabetes management difficult. Numerous studies have been reported globally that demonstrate significant differences between serum electrolyte and mineral levels among diabetic subjects than non-diabetic controls. Reduced serum magnesium and calcium levels have been linked to increased risks of cardiovascular complications; elevated potassium levels may contribute to arrhythmias. Yet, such data pertaining to the Pakistani population are scarce[5, 6].

The prevalence and implications of electrolyte and mineral imbalances within the unique socioeconomic and dietary context of Pakistan, coupled with the challenges of limited healthcare access in rural areas, are critical for effective diabetes management. This study provides a cross-sectional analysis of serum Na^+, K^+, Cl^-, Ca^{2+}, and Mg^{2+} levels in diabetic and non-diabetic individuals. The results reveal significant correlations between these imbalances and factors such as glycemic control, disease duration, and demographic characteristics[7]. Evidence-based recommendations derived from the findings aim to enhance clinical management and outcomes for diabetic populations. This study adds to the growing body of literature on electrolyte disturbances in diabetes and offers actionable insights for healthcare providers to optimize treatment strategies[8].

MATERIAL AND METHODS
Study Design and Setting: A Multicenter cross-sectional study was conducted from January 2022 to December 2022, this cross-sectional study was carried out in two tertiary care hospitals in Bakhtaran Amin Medical & Dental College, Multan and Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan. These hospitals serve a diverse patient population, and provide an appropriate setting to study urban and semi urban residents in Pakistan.
Study Population and Sampling: A systematic random sampling technique was used to recruit 300 participants (150 diabetics and 150 non diabetics) aged 30–70 years. Diabetic group inclusion criteria were a confirmed diagnosis of T2DM with a minimum disease duration of one year and regular follow-up in diabetes clinics. Age and sex matched non-diabetic controls were excluded

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if they had a history of chronic illness, use of medication affecting electrolytes, or had been recently hospitalized.

Data Collection Procedures: Sociodemographic information (age, sex, education, occupation), lifestyle factors (physical activity, dietary habits, smoking, alcohol consumption) and medical history (duration of diabetes, comorbidities, medications) were collected using a structured questionnaire, for participants. Body weight, height, and blood pressure were recorded by using calibrated instruments. Weight was calculated in kg divided by height in m2.

Laboratory Investigations: All participants were then given informed consent, and fasting venous blood samples (10 mL) were collected from all participants. Serum was separated from the samples by centrifuging the samples at 3500 rpm for 10 minutes and then stored at -80°C until analysis. Ion-selective electrodes and spectrophotometric methods on an automated chemistry analyzer were used to measure serum levels of sodium (Na^+), potassium (K^+), chloride (Cl^-), calcium (Ca^{2+}), and magnesium (Mg^{2+}). We measured fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) using glucose oxidase peroxidase method and high performance liquid chromatography (HPLC) respectively, to assess glycemic control.

Operational Definitions: Electrolyte imbalance was defined as serum levels outside the reference ranges: Na^+ (135–145 mmol/L), K^+ (3.5–5.5 mmol/L), Cl^- (96–106 mmol/L), Ca^{2+} (8.6–10.2 mg/dL), and Mg^{2+} (1.7–2.4 mg/dL). HbA1c > 8% was classified as poor glycemic control.

Data Quality Assurance: All measurements were repeated in triplicate, and internal quality controls were run daily. To minimize bias, laboratory staff were blinded to grouping of the participants. Prior to the study, data collectors were trained on standardized interview procedures.

Statistical Analysis: It was analyzed through SPSS version 26.0. Sociodemographic and clinical characteristics were computed as descriptive statistics. Mean ± standard deviation (SD) or median (interquartile range) was reported for continuous variables, as appropriate, based on normality, assessed by the Shapiro-Wilk test. Independent t tests or Mann–Whitney U tests were performed between group comparisons for continuous variables, and chi square tests were performed for categorical variables. To identify predictors of electrolyte imbalance, multivariable logistic regression models were used, adjusting for age, sex, BMI, glycemic control and disease duration. Statistically significant was considered a p value < 0.05.

Ethical Considerations: This study was strictly adhered to ethical considerations. All participants gave informed consent after being given a detailed explanation of the study purpose, procedures, potential risks, and benefits, and participation was entirely voluntary and not subject to coercion. The data was anonymized and all records were stored securely to prevent unauthorized access and confidentiality of participants' personal and medical information was maintained. Selection of the participants was done fairly with no discrimination by gender, socioeconomic status, and ethnicity. As far as it can, beneficence and nonmaleficence were maintained, protecting participants by reducing risks and avoiding harm. The study was approved by the Institutional Review Board (IRB) and conducted according to the principles of the Declaration of Helsinki and other relevant ethical guidelines. Participants were also informed they had the right to withdraw from the study at any time without negative consequences.

RESULTS

Participant Characteristics: The study included 300 subjects, 150 diabetic and 150 non-diabetic participants. Mean participant age was 53.2 ± 8.6 years (p = 0.42 between groups). Of the diabetics in this cohort, 62% had duration >5 years and 58% of poor glycemic control (HbA1c > 8%). Table 1 shows demographic and clinical characteristics.

Electrolyte and Mineral Profiles: Serum electrolyte and mineral levels were significantly different between diabetic and non-diabetic groups (Table 2). In diabetics blood levels of Na^+, Ca^{2+}, and Mg^{2+} were lower ($p < 0.001$) and K^+ and Cl^- higher ($p < 0.001$) than controls. Diabetics had more hyponatremia, hyperkalemia, hypocalcemia, and hypomagnesemia.

Prevalence of Electrolyte Imbalances: Electrolyte disturbance was significantly higher in diabetics (78.6%) than in non-diabetics (42.3%) ($p < 0.001$). Specific abnormalities included hyponatremia (41% vs 12%), hyperkalemia (27% vs 8%), hypocalcemia (38% vs 14%), and hypomagnesemia (47% vs 18%).

Correlations with Glycemic Control: Severe electrolyte disturbances were significantly associated with poor glycemic control (HbA1c > 8%). Multivariable regression revealed that for every 1% increase in HbA1c, the odds of hypomagnesemia increased by 23% (AOR: 1.The odds of hypocalcemia increased by 19% (AOR: 1.19, 95% CI: 1.05–1.35) ($p < 0.01$) and the odds ratio for developing hypocalcemia was 1.19 (95% CI: 1.05–1.36), $p < 0.01$.

Table 1: Demographic and Clinical Characteristics of Participants

Characteristic	Diabetic Group (n = 150)	Non-Diabetic Group (n = 150)	p-value
Age (years)	53.6 ± 8.7	52.8 ± 8.4	0.42
Male (%)	55	52	0.68
BMI (kg/m²)	27.8 ± 4.3	25.6 ± 3.9	0.03
HbA1c (%)	8.4 ± 2.2	5.3 ± 0.8	<0.001
Disease Duration >5y (%)	62	NA	-

Table 2: Serum Electrolyte and Mineral Levels

Parameter	Diabetic Group (Mean ± SD)	Non-Diabetic Group (Mean ± SD)	Reference Range	p-value
Sodium (Na+, mmol/L)	132.5 ± 4.2	137.3 ± 3.8	135–145	<0.001
Potassium (K+, mmol/L)	5.2 ± 0.5	4.3 ± 0.4	3.5–5.5	<0.001
Chloride (Cl-, mmol/L)	108.4 ± 3.1	102.7 ± 2.8	96–106	<0.001
Calcium (Ca2+, mg/dL)	8.6 ± 0.8	9.2 ± 0.6	8.6–10.2	<0.001
Magnesium (Mg2+, mg/dL)	1.5 ± 0.3	2.1 ± 0.4	1.7–2.4	<0.001

Table 3: Prevalence of Electrolyte Imbalances

Electrolyte Imbalance	Diabetic Group (%)	Non-Diabetic Group (%)	Odds Ratio (95% CI)	p-value
Hyponatremia	41	12	4.90 (2.76–8.69)	<0.001
Hyperkalemia	27	8	4.17 (1.98–8.81)	<0.001
Hypocalcemia	38	14	3.78 (2.11–6.78)	<0.001
Hypomagnesemia	47	18	4.05 (2.46–6.66)	<0.001

DISCUSSION

The results of this study show large deviations in serum electrolyte and mineral levels in diabetic patients of Pakistan and the systemic impact of diabetes on physiological homeostasis. These results are consistent with global literature, consistent with diabetes being a polygenic disorder that impacts critical biochemical pathways beyond glucose metabolism[9,10]. Compared with non-diabetic controls, diabetic individuals in this study had markedly lower sodium and calcium levels and higher potassium and chloride levels. The osmotic effects of chronic hyperglycemia result in shifting of fluid and electrolyte compartments, accounting for these findings. For the cohort, the causes of hyponatremia in diabetics 41% are dilutional effects of hyperglycemia and hyperkalemia can be explained by insulin deficiency, interfering with the Na+/K+ ATPase pump function[11]. Diabetic participants were strikingly hypomagnesemia and hypocalcemic. Nearly half of the diabetic group has magnesium depletion, which increases insulin resistance and poor control of glycemia[12]. Magnesium and calcium regulation is complex because these ions are essential for both neuromuscular and enzymatic functions and the interplay of the two underscores the complexity of mineral disturbances in diabetes[13]. Severe electrolyte imbalances were strongly associated with poor glycemic control, defined as HbA1c > 8%. This emphasizes the two way relationship between hyperglycemia and electrolyte disturbances. Chronic hyperglycemia accelerates renal losses of magnesium and calcium which is a positive feedback loop that perpetuates metabolic dysregulation[14,15]. Electrolyte imbalances in diabetics are very common and need to be monitored routinely as part of diabetes management. Dietary supplementation of magnesium and calcium as well as optimized glycemic control may reduce the risk of complications[16]. Early correction of electrolyte disturbances would be based on the strong association between electrolyte disturbances and cardiovascular risks and would potentially improve patient outcomes. Although they studied only urban tertiary care settings, the rural population may have been underrepresented. Furthermore, the cross-sectional design does not allow causal inference[17]. Temporal dynamics of electrolyte disturbances and their clinical sequelae need to be explored further in future longitudinal studies[18, 19].

CONCLUSIONS

The importance of obtaining comprehensive metabolic monitoring in diabetic care is emphasized in this study. The results highlight the need to correct electrolyte and mineral imbalances to avoid complications and to enhance the quality of life in the diabetic populations. Our results offer a basis for developing targeted interventions aimed at Pakistani patients who possess the distinctive sociodemographic and clinical characteristics.

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