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ORIGINAL RESEARCH

Assessment of Electrolyte Imbalance and Associated Factors Among Adult Diabetic Patients Attending the University of Gondar Comprehensive Specialized Hospital, Ethiopia: A Comparative Cross-Sectional Study

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Introduction: Electrolyte imbalance refers to altered electrolyte levels that predominantly affect diabetic patients due to hyperglycemia which rise plasma osmolality and impaired renal function, contributing to a change in electrolyte level. Therefore, this study aimed to assess the prevalence of electrolyte imbalance and its associated factors among diabetic patients and healthy control groups attending the University of Gondar Comprehensive Specialized Hospital.

Patients and Methods: A comparative cross-sectional study was conducted on 130 diabetic patients and 130 diabetes-free controls. Sociodemographic, behavioral and clinical data were collected using a structured questionnaire. After measuring anthropometric parameters, 5mL of the blood sample was collected. Electrolytes were measured based on ion-selective electrode methods. Fasting blood glucose, and creatinine were measured by spectrophotometric enzyme hexokinase, and Jaffe reaction methods, respectively. The data was entered into Epi-data version 4.6 and analyzed using STATA version 14. Mann–Whitney U-tests and independent t-tests were used for comparison. Multiple logistic regression analysis was done to determine the factors associated with electrolyte imbalances. P-value <0.05 was considered statistically significant.

Result: The overall prevalence of electrolyte imbalance among diabetic patients and controls were 83.07% and 52.31%, respectively. The mean of Na^+ and the median level of Mg^{2+} and Ca^{2+} were significantly decreased. However, the mean level of Cl^- was significantly increased in diabetic patients as compared to control groups. In multivariable logistic regression: alcohol consumption AOR = 3.34 [1.02–10.9], no formal education AOR = 5.38 [1.14–25.4], hyperglycemia AOR = 6.32 [2.04–19.5], and urbanization AOR = 5.6 [1.44–22.3] showed significant association with electrolyte imbalance.

Conclusion: Diabetic patients have more likely to develop electrolyte imbalance than control groups. Diabetic participants showed significantly reduced Na^+, Mg^{2+}, and Ca^{2+} levels and significantly increasing Cl^- levels when compared to control groups. Hyperglycemia, alcohol drinking habits, urbanization, and no-formal education were statistically significantly associated with electrolyte imbalance.

Keywords: electrolyte imbalance, diabetes mellitus, associated factors, Ethiopia

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Introduction

Electrolytes are electrically charged molecules that are required for normal metabolic reactions and homeostasis. Electrolytes sustain cell membrane functions, neuron conductivity, muscle contractility, hormone action, bone structure, and fluid and acid-base balance. Electrolyte imbalance occurs when the electrolyte level is abnormally high or low than the normal range as a result of a variety of pathophysiological factors, including nutritional status, concurrent acid-base imbalances, pharmaceuticals, other co-morbid disorders (mostly renal disease), or acute illness.[1,2]

Electrolyte imbalance predominantly affects diabetic people due to osmotic fluid changes brought on by hyperglycemia, and it has two important effects on the body's electrolyte concentration. If water movement transports intracellular electrolytes to the extracellular space, it may have a dilutional effect, by lowering extracellular electrolyte concentrations or increasing extracellular concentrations, especially in an insulin-deficient state.[3–5]

These osmotic effects dilute serum sodium (Na^+) levels, potentially resulting in hyponatremia (a serum Na^+ concentration less than 135 mmol/L).[5] The activity of the Na^+/K^+ ATPase depends on insulin. The transmembrane Na^+ and K^+ gradients are kept in place by this transporter. In diabetics with insufficient insulin production or insulin resistance, the activity of this transport protein may be reduced. Cellular K^+ diffusion out of cells and cellular Na^+ diffusion in cells are governed by trans-membrane electrical gradients. Changes in insulin levels of the hormone have an impact on serum electrolyte levels.[6,7]

Level of Magnesium (Mg^{2+}) less than 1.7 mg/dL is a common complication of diabetes and is brought on by an insulin-resistant condition, or poor glycemic control. Insulin resistance may decrease the transient receptor potential of melastatin 6 (TRPM6) expression in the kidneys, which in turn may increase urine Mg^{2+} loss and decrease plasma Mg^{2+} concentration. Coexisting with hypomagnesemia also leads to hypokalemia as a result of decreased intracellular Mg^{2+}, which reduces the magnesium-mediated control of renal outer medullary potassium channel (ROMK channels, and contributes to K^+ waste.[8,9] Reduced renal PO_4^- reabsorption via the Na-Pi transporters in the renal proximal tubule is one of the mechanisms causing hypophosphatemia (serum PO_4^- level less than 2.5 mg/dL) in diabetic individuals (due to acidosis and hyperglycemia).[10,11]

Diabetes mellitus is a serious public health problem linked to non-communicable diseases. It is the world's largest pandemic, and its rapidly rising prevalence rate is a cause for concern.[12] According to the International Diabetes Federation (IDF), diabetes was the cause of death for 6.7 million people worldwide in 2021, with 537 million adults suffering from the disease. By 2030, this number is predicted to rise to 643 million.[13] DM is known to be like electrolyte imbalance which affects both community individuals and a wide range of patients (from asymptomatic to severely ill).[14] Diabetes patients frequently experience hyponatremia, which increases morbidity and mortality.[15] In non-hospitalized DM patients, hypomagnesemia has been documented to occur in 11–47.7% of cases. Diabetes patients with hypomagnesemia develop their disease more rapidly and are more likely to experience complications from their diabetes. This includes macrovascular conditions including peripheral artery disease and cardiovascular disease.[9,16]

When compared to the cost of normonatremic participants in the United States, hyponatremia was related to up to almost $3000 greater hospital costs per patient. It also has a higher economic cost and a higher risk of readmission.[17] Electrolyte imbalance affects the management and progression of DM, which can be fatal in severe situations. Poor plasma Na^+ management has been associated with two diseases with potentially fatal consequences (cerebral edema and osmotic demyelination syndrome). Renal impairment is frequently seen in people with DM, and this condition itself is an independent risk factor for hyperkalemia. Variations in K^+ levels can cause dysrhythmias, impair the electrical conduction of the heart, and even result in sudden death.[1,18] Electrolyte imbalance should be considered a serious illness, especially in diabetes patients, because these problems frequently occur in diabetic patients. However, there is a limited amount of information on the electrolyte profile of diabetic patients in Ethiopia.

Materials and Methods
Study Population, Area, Design, and Period

An institution-based cross-sectional study design and systematic random sampling techniques were used to carry out the study. The study was conducted at the UoGCSH. The hospital is located approximately 738 km northwest of Addis

Ababa and 180 km north of Bahir Dar in central Gondar administrative zone of the Amhara regional state. The study was conducted from April 13, 2022, to June 15, 2022. All types of diabetic patients attending UoGCSH during the study period and who fulfilled the inclusion criteria of the study were included. Age and sex-matched healthy individuals who come to UoGCSH were also included as controls. Controls were interviewed for prior history of diabetes and fasting blood sugar was measured to make sure it is in the normal range.

Eligibility Criteria
Inclusion Criteria
The inclusion criteria were adult diabetic patients who were willing to voluntarily participate in the study. All adult healthy individuals who were willing to participate in the study were included in the control groups.

Exclusion Criteria
Those study participants having known kidney disease, mental illness, pregnant diabetes patients, persistent diarrhea and vomiting, thyroid disorder, malignancy, diuretics users, and acute illness were excluded by reviewing their medical records and performing screening.

Sample Size Determination and Sampling Technique
The sample size was determined by using the double proportion formula. Open Epi, version-7 software was used by considering the following assumptions; a study done at Benin reported the proportion of at least one electrolyte abnormality for case groups (P_1=41.3%) and control groups (P_2=16.4%).[19] Power (80%), r = ratio of control to case (1:1), and 95% CI. This gives a total of 236 after adding 10% non-response rate, 130 diabetes cases and 130 healthy controls were enrolled. A systematic sampling technique was employed to select study participants at UoGCSH.

Operational and Standard Definitions
Electrolyte imbalance; test results showing a changed level of at least one of the electrolytes (K^+, Cl^-, Na^+, Ca^{++}, Mg^{++}, or PO_4^-).[2] The following ranges were used to determine the imbalance for each electrolyte based on the reference range of the central laboratory of UoGCSH: Na^+= 135–145 mmol/L, K^+= 3.5–5.5 mmol/L, Ca^{2+}= 2.1–2.55 mmol/L, Cl^- = 98–107 mmol/L, Mg^{2+} =1.7–2.8 mg/dL, and PO_4^-= 2.5–4.6 mg/dl.

Body mass index is weight in kilogram divided by height in meter square and the diabetic patients will be classified as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30 kg/m^2) based on WHO guideline category.[20]

Hypertension: hypertension is based on an average systolic BP (SBP) ≥140 mm Hg, diastolic BP (DBP) ≥90 mm Hg, or self-reported use of antihypertensive medication.[21]

Alcohol intake: Alcohol consumption is classified as non-drinkers (those who never drink any alcohol), regular drinkers (those who drink alcohol at least one day per week), and ex-drinkers (those who do not currently consume alcohol but have drunk alcohol in the past).[22]

Glycaemic control – fasting blood glucose (FBG) level, participants will be classified as with good glycaemic control (FBG <130 mg/dl) and poor glycaemic control (FBG ≥130 mg/dl).[23]

Data Collection and Laboratory Methods
The sociodemographic characteristics of study participants were collected by using a semi-structured questionnaire prepared for this study. Data for these characteristics were collected by trained nurses through a face-to-face interview. The study participants were interviewed after written informed consent was taken. Height and weight were measured by using a stadiometer and bio-electrical impedance (Seca Deutschland, Germany) instruments, respectively. During the measurement of height and weight, the study participants were asked to remove their shoes, hats, and any bulky clothing, and the participants were asked to look straight ahead, face forward, with the reader's eye at the level of the headpiece. Then the height and weight were recorded. The body mass index (BMI) was calculated as weight divided by height

square (kg/m^2) and blood pressure (BP) was measured by using a Mercury sphygmomanometer from the left upper arm and positioned at the heart level.

Three successive blood pressure readings at an interval of at least one minute mean blood pressure was taken. After receiving informed consent from the study participants, 8–12 hours of fasting 5mL of venous blood was collected preferably at the antecubital area by applying a tourniquet. Before collecting the sample, the puncture area of the vein was disinfected by using 70% alcohol. The serum was collected using a serum separator tube at the medical ward department of UoGCSH. After collection, specimens were transported to the clinical chemistry unit of the UoGCSH laboratory for analysis. The collected blood sample was left for 30 minutes at room temperature. Then the blood samples were centrifuged for 5 minutes at 3500 revolutions per minute (rpm) to separate serum from formed elements. All these procedures were done by the laboratory technologist and principal investigator by applying standard operating procedures (SOPs). Electrolytes (Na$^+$, K^{2+}, Ca^{2+}, Mg^{2+}, Po$_4$$^-$, and Cl$^-$) and concentration of FBS and creatinine were determined by Beckman Coulter DXC 700 AU and 600 AU (Danaher Corporation company, USA), respectively.

Data Quality Assurance and Management

After the completion of each questionnaire, cross-checking was done between the data collector and principal investigator to assure the completeness of the data collected. The label on the test tube and the study participants' unique identification number on the questionnaire were checked. Before patient sample processing, quality controls were performed, and the study participants' result was taken after confirmation of the controls results are within acceptable range.

Data Analysis and Interpretation

The data was checked for completeness and then inserted into EPI data version 4.6, then transferred to STATA version 14 for analysis. The model of fit was checked by Hosmer and Lemeshow's goodness-of-fit statistic. The Kolmogorov–Smirnov and Shapiro–Wilk normality tests and skewness were conducted to check the normality of continuous variables. For continuous variables, Mann–Whitney U-tests for abnormally distributed data were used to determine the difference in medians. Independent t-tests were used to determine the mean difference for normally distributed data. The mean±SD was used to represent data with a normal distribution, while the medians and IQR were used to represent data with an abnormal distribution. Binary logistic regression was used to identify associated factors for electrolyte imbalance in DM, and variables with P-values of less than 0.25 were selected and shifted to multivariable logistic regression with an adjusted odds ratio. Variables with a P-value of less than 0.05 were considered statistically significant.

Ethical Consideration

Ethical clearance was obtained from research and ethical review committee of School of Biomedical and Laboratory Sciences, college of medicine and health sciences University of Gondar. Ethics approval number for the study is Ref No. SBMLS/271/2022. The study was conducted following the Declaration of Helsinki. Permission letter was also obtained from UoGCSH medical director. To ensure confidentiality of the study participant's information and codes were used so that the name and any identifier of participants was not used on the questionnaire and laboratory requests. Data were collected after written informed consent was given for each participant. The collected data was not used for another purpose other than the present study. Participants with abnormal test results were communicated through data collectors and linked to University of Gondar comprehensive Specialized Hospital for treatment.

Result

Sociodemographic, Behavioural, and Anthropometric Characteristics of Study Participants

This study included 130 diabetic patients and 130 healthy control groups, with a response rate of 100%. Among the study groups, 138 (53.307%) were females. One hundred and fifty-seven (60.38) ranged from 40 to 64 years old. One hundred and ninety (73.07%) of study participants were urban residents, and 115 (44.2%) were married. Based on educational

status, 105 (40.4%) had no formal education and 79 (30.38%) of those were public servants. Based on the lifestyle conditions 134 (51.1%) study participants had alcohol-drinking habits. One hundred and ninety (73.07%) of them were in the normal range of BMI level. Of all study participants, 227 (87.3%) and 236 (90.8%) had normal systolic and diastolic blood pressure, respectively (Table 1).

Table 1 Socio-Demographic, Behavioural, and Anthropometric Characteristics of Participants (n = 260, UOGCSH, Gondar, 2022), Pearson's Chi-Square Test)

Variables		Study Participants (n=260)			
		Diabetic Patients (n=130)	Control Groups (n=130)	Total (n=260)	p-value
Age	27–39	33 (25.38)	38 (29.23)	71 (27.3)	0.895
	40–64	83 (63.84)	74 (56.9)	157 (60.38)	
	65–76	14 (10.7)	18 (13.8)	32 (12.3)	
Sex	Female	69 (53.08)	69 (53.08)	138 (53.07)	0.578
	Male	61 (46.92)	61 (46.92)	122 (46.92)	
Residence	Urban	105 (80.77)	85 (65.38)	190 (73.07)	0.476
	Rural	25 (19.23)	45 (34.62)	70 (26.92)	
Marital status	Single	43 (33.08)	45 (34.6)	88 (33.8)	0.343
	Married	56 (43.08)	59 (45.4)	115 (44.2)	
	Divorced	14 (10.77)	12 (9.23)	26 (10)	
	Widowed	17 (13.08)	14 (10.7)	31 (11.9)	
Education status	No formal education	54 (41.5)	51 (39.2)	105 (40.4)	0.017
	Primary school	23 (17.69)	15 (11.5)	38 (14.6)	
	Secondary school	22 (16.9)	26 (20)	48 (18.46)	
	College and university	31 (23.8)	38 (29.2)	69 (26.5)	
Occupation	Public servant	40 (30.77)	39 (30.00)	79 (30.38)	0.038
	Merchant	33 (25.38)	35 (26.92)	68 (26.15)	
	Farmer	21 (16.15)	46 (35.38)	67 (25.76)	
	Unemployed	20 (15.38)	0	20 (7.69)	
	Housewife	16 (12.31)	10 (7.69)	26 (10)	
Physical activity	Yes	21 (16.15)	35 (26.92%)	56 (21.5)	0.07
	No	109 (83.85)	95 (73.08)	204 (78.4)	
Alcohols drinking	Yes	64 (49.2)	70 (53.8)	134 (51.5)	0.028
	No	66 (50.7)	60 (46.1)	126 (48.4)	
Cigarette smoking	Yes	0	1 (0.77)	1 (0.4)	0.489
	No	130 (100)	129 (99.23)	259 (99.6)	

(*Continued*)

Table 1 (Continued).

Variables		Study Participants (n=260)			
		Diabetic Patients (n=130)	Control Groups (n=130)	Total (n=260)	p-value
Body mass Index	Underweight	9 (6.92)	13 (10.0)	22 (8.5)	0.04
	Normal	76 (58.46)	114 (87.69)	190 (73.07)	
	Overweight	35 (26.92)	2 (1.54)	37 (14.2)	
	Obese	10 (7.69)	1 (0.8)	11 (4.23)	
Systolic blood pressure	<140 mmHg	97 (74.6)	130 (100)	227 (87.3)	0.194
	≥140mmHg	33 (25.4)	0	33 (12.7)	
Diastolic blood pressure	<90mmHg	106 (81.5)	130 (100)	236 (90.8)	0.243
	≥90mmHg	24 (18.5)	0	24 (9.2)	
Presence of comorbidity	Hypertension	46 (35.38)	0	46 (17.7)	
	Cardiovascular disease	0	0	0	
	Renal diseases	0	0	0	
Duration of DM	<10 years	87 (67.2%)	0	87 (33.4%)	
	≥10 years	43 (33.1%)	0	43 (16.5%)	

Abbreviations: DM, diabetes mellitus; n, number; mmHg, millimeter mercury.

Prevalence of Electrolyte Imbalance Among Diabetic Patients and Control Group

In diabetic patients, the prevalence of electrolyte imbalance in at least one of the parameters among the six electrolyte parameters was 83.07% (108/130), (95% CI: 75.5–88.6%) among cases and 52.31% (68/130), (95% CI: 43.6–60.9%) among control groups. The prevalence of electrolyte imbalance among diabetic patients was 51 (39.2%) hyponatremia, 41 (31.5%) hypomagnesemia, 35 (26.9%) hyperchloraemia, 30 (23.0%) hypophosphatemia, and 29 (22.3%) hypokalaemia. Whereas the prevalence of electrolyte imbalance among control groups was 22 (16.9%), 15 (11.5%), and 11 (8.46%), hypophosphatemia, hyperchloraemia, and hypocalcemia, respectively (Table 2).

Table 2 Prevalence of Electrolyte Imbalance Among Diabetic Patients and Control Group (n = 260, UOGCSH, Gondar, 2022)

Electrolytes	Categories	Diabetic Patients		Control Groups		Total	
		n (%)	CI (95%)	n (%)	CI (%)	n (%)	CI (95%)
Sodium (Na+)	Hyponatremia	51 (39.2)	31.1–47.9	9 (6.92)	3.61–12.9	60 (23.2)	18.3–28.6
	Hypernatremia	15 (11.4)	7.02–18.3	9 (6.92)	3.61–12.9	24 (9.23)	6.25–13.4
	Normonatremia	64 (49.2)	40.6–57.9	112 (86.2)	78.9–91.2	176 (67.7)	61.7–73.1
Potassium (K+)	Hypokalemia	29 (22.3)	15.9–30.4	5 (3.84)	1.59–9.0	34 (13.1)	9.47–17.8
	Hyperkalemia	12 (9.2)	5.71–15.7	2 (1.59)	0.37–6.04	14 (5.38)	3.2–8.91
	Normokalemia	89 (68.5)	59.9–75.9	123 (94.6)	89.0–97.4	212 (81.5)	76.3–85.8

(*Continued*)

Table 2 (Continued).

Electrolytes	Categories	Diabetic Patients		Control Groups		Total	
		n (%)	CI (95%)	n (%)	CI (%)	n (%)	CI (95%)
Chlorine (Cl-)	Hypochloremia	10 (7.69)	4.15–13.8	4 (3.08)	1.14–8.0	14 (5.38)	3.2–8.91
	Hyperchloremia	35 (26.9)	19.9–35.3	15 (11.5)	7.03–18.4	50 (19.23)	14.9–24.5
	Normochloremia	85 (65.4)	56.7–73.1	111 (85.4)	78.1–90.5	196 (75.4)	69.7–80.3
Calcium (Ca2+)	Hypocalcaemia	20 (15.4)	10.1–22.8	11 (8.46)	4.71–14.7	31 (11.9)	8.49–16.5
	Hypercalcaemia	16 (12.3)	7.63–19.3	6 (4.62)	2.06–9.10	22 (8.46)	5.6–12.5
	Normocalcaemia	94 (72.3)	63.8–79.4	113 (86.9)	79.9–91.8	207 (79.6)	74.2–84.1
Magnesium (Mg2+)	Hypomagnesemia	41 (31.5)	24.0–40.1	5 (3.85)	1.59–9.00	46 (17.69)	13.5–22.9
	Normomagnesemia	89 (68.5)	59.9–75.9	125 (96.2)	90.9–98.4	214 (82.3)	77.1–86.5
Phosphate (Po4-)	Hypophosphatemia	30 (23.0)	16.6–31.2	22 (16.9)	11.4–24.5	52 (20.0)	15.5–25.3
	Normophosphate	100 (76.9)	68.8–83.4	108 (83.1)	75.5–88.7	208 (80.0)	74.7–84.4
Total electrolyte imbalance		108 (83.07)	75.5–88.6	68 (52.3)	43.6–60.9	176 (67.7)	61.7–73.1

Abbreviations: CI, Confidence Interval; n, number.

Factors Associated with Electrolyte Imbalance Among Diabetes Patients and Controls

After performing bivariable regression analysis, alcohol drinking habits, occupation, body mass index, educational status, and presence of diabetes reported significant association with EI. Diabetic patients were 4.60 [AOR = 4.60, 95% CI = 2.28–9.24, P = 0.000] times more likely to develop electrolyte imbalance than non-diabetic patients, and alcohol drinkers were 2.06 [AOR = 2.06, 95% CI = 1.15–3.70, P = 0.015] times more likely to develop electrolyte imbalance than non-alcohol drinkers in multivariable regression with P-value <0.05 (Table 3).

Table 3 Bivariate and Multivariable Logistic Regression Analysis of Factors Associated with Electrolyte Imbalance Among Study Individuals (n = 260, UOGCSH, Gondar, 2022)

Variables		EI		COR (95%)	p-value	AOR (95%)	P-value
		Yes	No				
Educational status	No formal education	77	28	1.79 (0.82–3.91)	0.143	1.65 (0.65–4.19)	0.288
	Primary	23	15	1		1	
	Secondary	28	20	0.91 (0.38–2.17)	0.837	1.04 (0.38–2.83)	0.930
	College and university	48	21	1.49 (0.65–3.41)	0.345	1.07 (0.32–3.57)	0.910
Occupation	Public servant	58	21	1.46 (0.56–3.77)	0.433	1.99 (0.57–6.96)	0.279
	Merchant	38	30	0.67 (0.26–1.71)	0.404	0.79 (0.28–2.21)	0.659
	Farmer	45	22	1.08 (0.41–2.81)	0.870	1.35 (0.45–4.00)	0.588
	Unemployed	18	2	4.76 (0.89–25.28)	0.067	2.37 (0.41–13.7)	0.332
	Housewife	17	9	1		1	

(*Continued*)

Table 3 (Continued).

Variables		EI		COR (95%)	p-value	AOR (95%)	P-value
		Yes	No				
Alcohol drinking	Yes	99	35	1.8 (1.06–3.04)	0.029	2.06 (1.15–3.70)	0.015*
	No	77	49	1		1	
BMI	Underweight	11	11	0.52 (0.21–1.26)	0.149	0.46 (0.17–1.23)	0.126
	Normal	125	65	1		1	
	Overweight	40	8	2.6 (1.14–5.88)	0.022	1.11 (0.42–2.91)	0.817
Presence of dm	Yes	108	22	4.47 (2.52–67.9)	0.000	4.60 (2.28–9.24)	0.000*
	No	68	62	1		1	

Note: *Significant association.

Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; EI, electrolyte imbalance; SBP, systolic blood pressure; DBP, diastolic blood pressure; 1, reference category.

Factors Associated with Electrolyte Imbalance Among Diabetic Patients

After performing bivariable analysis fasting blood glucose, alcohol drinking, residence, educational status, and medication of DM showed significant association with EI.

In multivariable analysis, hyperglycemia diabetic patients were 6.32 [AOR: 6.32, 95% CI = 2.04–19.59, P = 0.001] times more likely to develop an electrolyte imbalance as compared to normoglycemic. Diabetic patients who had alcohol drinking habits were 3.34 [AOR: 3.34, 95% CI = 1.02–10.9, P = 0.046] times more likely to develop EI compared to non-drinkers. Diabetic patients who had no formal education had 5.38 [AOR; 5.38, 95% CI = 1.14–25.4, P = 0.033] time more likely to develop electrolyte imbalance as compared to those with higher educational status, and diabetic patients who lived in urban areas were 5.67 [AOR: 5.67, 95% CI = 1.44–22.3, P = 0.013] time more likely to develop electrolyte imbalance as compared to rural residents (Table 4).

Table 4 Bivariate and Multivariable Logistic Regression Analysis of Factors Associated with Electrolyte Imbalance Among Diabetic Patients (n = 130, UOGCSH, Gondar, 2022)

Variable		EI		COR (95%)	p-value	AOR (95%)	p-value
		Yes	No				
Residence	Urban	91	14	3.05 (1.11–8.40)	0.030	5.67 (1.44–22.30)	0.013*
	Rural	17	8	1		1	
Educational status	No formal education	48	6	2.82 (0.80–9.94)	0.106	5.38 (1.14–25.40)	0.033*
	Primary	17	6	1		1	
	Secondary	17	5	1.2 (0.30–4.69)	0.793	1.91 (0.39–9.20)	0.417
	College and university	26	5	1.83 (0.48–6.97)	0.37	2.52 (0.49–12.79)	0.262
Alcohol drinking	Yes	58	6	3.09 (1.12–8.50)	0.029	3.34 (1.02–10.93)	0.046*
	No	50	16	1		1	

(*Continued*)

Table 4 (Continued).

Variable		EI		COR (95%)	p-value	AOR (95%)	p-value
		Yes	No				
Medication of dm	Oral	61	10	1.69 (0.31–4.17)	0.387	2.32 (0.53–10.23)	0.263
	Insulin	29	7	1.15 (0.51–5.59)	0.831	1.33 (0.26–6.74)	0.728
	Mixed medication	18	5	1		1	
FBS	Hyperglycaemic	91	10	6.42 (2.39–17.2)	0.000	6.32 (2.04–19.59)	0.001*
	Normoglycaemic	17	12	1		1	

Note: *Significant association.
Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; FBS, fasting blood glucose; 1, reference category.

Comparison of Electrolyte Level Among Diabetic Patients and Control Groups

After checking the distribution of variables, we used both *t*-tests and Mann–Whitney *U*-tests to compare the mean and median variables, respectively. The mean levels of serum Na^+ and Cl^- showed statistically significant differences between diabetic patients and control groups (P < 0.05). The median level of serum K^+ and PO_4^- did not show a statistically significant difference between diabetic patients and control groups (P = 0.176 and P = 0.142, respectively). But the median serum level of Mg^{2+} and Ca^{2+} showed a statistically significant difference between diabetic patients and control groups (P < 0.05) (Table 5 and Table 6).

Discussion

This study showed that the majority of the diabetic patients had a high prevalence of one or more electrolyte imbalances when compared with the control subjects 83.07%, and 52.31%, respectively. Hyponatremia was the most common abnormality among the serum electrolytes measured in diabetic patients, with a prevalence of 39.2% [95% CI: 31.1–47.9] similar to those

Table 5 Mean Comparison of Electrolytes Parameters Between Diabetic Patients and Control Groups (*t*-test) (n = 260, UOGCSH, Gondar, 2022)

Variable	Diabetic Patients (mean ± SD)	Control Groups (mean± SD)	p-value
Na^+	136.8 ± 5.79	139.7±3.3	<0.001*
Cl-	105.13 ± 3.76	104.04 ± 3.45	0.0079*

Note: *Statistically significant.
Abbreviations: Na+, sodium, Cl-, chloride.

Table 6 Median Comparison of Electrolytes Parameters Between Diabetic Patients and Control Groups (Mann-Whitely *U*-Test) (n = 260, UOGCSH, Gondar, 2022)

Variables	Diabetic Patients Median (IQR)	Control Groups Median (IQR)	p-value
K^+	4.1 (3.5, 4.6)	4.2 (3.8, 4.4)	0.176
Mg^{2+}	1.9 (1.5, 2.2)	2.2 (2.0, 2.5)	0.001*
PO_4^-	3.1 (2.5, 3.9)	3.3 (2.7, 4.2)	0.142
Ca^{2+}	2.3 (2.2, 2.4)	2.4 (2.2, 2.5)	0.045*

Note: *Statistically significant.
Abbreviations: K^+, potassium; Mg^{2+}, magnesium; Ca^{2+}, calcium; PO_4^-, phosphates.

reported in Ethiopia (40.6%), Southern India (33%), and Benin (45.3%).[6,24,25] Due to the osmotically active nature of glucose, diabetes can cause a drop in serum Na^+ levels by causing a dilution effect that moves water from intracellular to extracellular compartments.[26] However, our study finding was lower than studies done in Bangladesh (63.3%) and Kerala (75%).[27,28] The difference could be those studies done in admitted diabetic patients included diuretics medication takers and the majority of participants had diabetic nephropathy, both of which are major contributors to hyponatremia. This study also showed that there was hypernatremia of 11.4% [95% CI: 7.02–18.3] due to osmotic diuresis increasing urination if the water is not replaced sufficiently leading to hypernatremia.[4] Our result is consistent with Benin (17.3%) and Nigeria (15.6%).[24,29]

The secondary electrolyte imbalance in our study was hypomagnesemia with 31.5% [95% CI: 24.0–40.1]. Our finding is consistent with the prevalence of hypomagnesemia in the Netherlands (30.6%).[30] Hypomagnesemia might be associated to decreased tubular Mg^{2+} reabsorption brought on by insulin resistance.[31] While our finding was lower than Pakistan (57.3%), Nepal (50%), and India (44%).[9,32,33] Variation in the targeted groups may be related to dietary habits, the severity of DM, and the heterogeneity of the selected patient.

The study also reported hyperchloremia and hypochloremia of 26.9% [95% CI: 19.9–35.3] and 7.69% [95% CI: 4.15–13.8], respectively. Our finding inconsistency with Southern India and Nigeria studies reported hyperchloremia and hypochloremia was (2.7% vs 31%) and (8.9% vs 40.1%).[25,29] The difference could be that studies performed on hospital admitted diabetic patients having high-risk factors such as vomiting and excessive diuretic use, as well as diabetic neuropathy which is the most common cause of hypochloremia, whereas in our study hyperchloremia was higher than those studies because ketoacidosis lowers blood pH, upsetting the acid-base balance and elevating Cl^- levels. Diabetic ketoacidosis may be responsible for the rise in Cl^- levels in DM patients.[34]

Our study also showed the prevalence of hypophosphatemia which is 23% [95% CI: 16.6–31.2], and it is similar to Ukraine study (21.8%).[35] Decreased renal phosphate reabsorption via the Na-Pi transporters in the renal proximal tubule (due to acidosis and hyperglycemia). Phosphorus moves from the extracellular to the intracellular compartment during insulin therapy, resulting in hypophosphatemia.[36] This study also showed the prevalence of hypokalemia, and hyperkalemia 22.3% [95% CI: 15.9–30.4] and 9.23% [95% CI: 5.71–15.7] in diabetic patients, respectively. Changes in intracellular Mg^{2+} concentration can lead to hypokalemia in diabetics, and insulin therapy can also promote the K^+ shift into cells.[37] On the other hand, hyperglycemia causes a redistribution of K^+ from the intracellular to extracellular fluid compartment due to factors that impair cellular uptake, leading to hyperkalemia.[27] Our funding is greater than the prevalence of hypophosphatemia in Jordan (10%),[11] as well as hypokalemia and hyperkalemia in Thailand (6.7% and 2.9%), respectively.[38] This discrepancy may be explained by the sociodemographic differences among the study participants, including their levels of education and living conditions.

In our study, the prevalence of hypocalcemia and hypercalcemia were 15.3% (95% CI: 10.1–22.8) and 12.3% (95% CI: 7.63–19.3), respectively. Hypercalcemia in diabetic patients may be caused by hypophosphatemia and increased renal calcium absorption, hypocalcemia due to renal failure in diabetic individuals is linked to hypomagnesemia.[39] Our finding is much lower than the prevalence of hypocalcemia and hypercalcemia reported in Benin (41.3% vs 23.3%) and Cameron (48% vs 30%), respectively.[19,24] The disparity might be due to the diversity of the targeted populations, and it might be related to the severity of DM cases.

The mean serum level of Na^+ (136.8±5.79 vs 139.7±3.), P = 0.001 was significantly decreased in diabetic patients when compared to control groups. This result is similar to the finding of different studies in Saudi, Nigeria, Sudan, Iraq, and China.[34,40–43] Because hyperglycemia causes water to be driven out of intracellular fluids, sodium levels are reduced through dilution, and elevated glucose levels reduce Na^+-K^+-ATPase activity, which is thought to be linked to hyponatremia.[5,7]

The mean level of Cl^- was significantly higher than control groups (105.13±3.76vs104.04±3.45). This result is in line with those studies in India and Iraq[42,44] but it is inconsistent with a study conducted in Kerala.[28] Elevated serum Cl^- levels in diabetic patients may be caused by a drop in blood pH brought by ketoacidosis, which causes an acid-base imbalance that results in elevated Cl^- levels.[34]

The median Ca^{2+} levels were significantly reduced in participants with DM compared to control groups. Our result is supported by those findings conducted in Nigeria, China, and India.[43,45,46] Due to hyperglycemia, which is common in DM patients, can cause varying degrees of renal impairment, which can then result in poor phosphorus clearance and eventually build in the blood and bind Ca^{2+}, causing hypocalcemia. Additionally, hypomagnesemia can also cause hypocalcemia.[39]

The median level of Mg^{2+} concentration was significantly decreased in diabetic patients than in control groups. Our findings were comparable with a study done in Pakistan and India.[32,47] Due to insulin's role in regulating Mg^{2+} reabsorption in the kidney through the TRPM 6 channel. Insulin resistance or insulin deficit decreased renal magnesium absorption by blocking the TRPM 6 channel, which led to urine magnesium wasting.[48]

Educational level was also found associated with electrolyte imbalance. It was found that DM patients had no formal education 5.3 higher odds of having electrolyte imbalance among diabetic patients [AOR: 5.38; 95% CI: 1.14.–25.40, P = 0.033] when compared to those patients with higher education status. This finding was in agreement with a study done in Ethiopia.[2] The rationale might be people with higher levels of education are more likely to be aware of using health services than those with lower levels. Additionally, knowledge is essential for unlocking any closed doors to life in the world and enabling everyone to live a healthy lifestyle through behavioral modification.

The participants who lived in urban were five times more likely [AOR: 5.67, 95% CI: 1.44–22.30] to develop electrolyte imbalance than those who lived in rural. There may be several explanations for this including a shift in diet with greater consumption of sugar and saturated fat, as well as a more sedentary lifestyle and increased alcohol use, which are observed globally. Overall, urbanization could have exacerbated DM causing an electrolyte imbalance.[49]

Electrolyte imbalance was 3.34 times more common in alcoholics than non-alcoholics [AOR: 3.34, 95% CI: 1.02–10.93, P = 0.046] this finding was agreed with studies done in Ethiopia and Southern India.[2,50] Alcohol exposure can cause a variety of electrolyte imbalances such as hypophosphatemia, hypomagnesemia, and hypokalemia multiple factors were identified as the causes of this, including inadequate nutrition, increased excretion through increased urine osmolality, internal redistribution, and decreased tubular cell reabsorptive ability.[2,51,52]

Patients with hyperglycemic had increased the likelihood of electrolyte imbalance by 6.3 times more than patients with normoglycemic [AOR = 6.32, 95% CI: 2.04–19.59, P = 0.001]. Similar findings were reported from Ethiopia, Bangladesh, and Nepal.[6,27,53] The plausible explanation could be that elevated blood sugar levels cause hyperosmolarity, which shifts fluids and causes intracellular dehydration and electrolyte loss. Na^+ and K^+ are the two electrolytes that are most significantly reduced. A dispersed electrolyte concentration results from the body's attempt to eliminate blood glucose by increasing urine production.[4,5]

The odds of electrolyte imbalance in diabetic patients were 4.60 times higher than in control groups (AOR = 4.60; 95% CI, 2.28–9.24, P = 0.000). This is due to several underlying mechanisms that have been proposed for electrolyte imbalance in DM due to hyperglycemia-induced osmotic fluid shifts or to total-body deficits brought about by osmotic diuresis. Complications of diabetic nephropathy and certain medications used in the management of diabetes may also contribute to electrolyte imbalance.[4,5]

Conclusion

In conclusion, diabetic patients have more likely to develop electrolyte imbalance than control groups. Diabetic participants showed a significantly decreasing Na^+, Mg^{2+}, and Ca^{2+} level and a significantly increased level of Cl^- when compared to control groups. There was a statistically significant association of hyperglycemia, alcohol drinking habits, urbanization, and education status with electrolyte imbalance.

Recommendation

Routing monitoring and assessment of serum electrolyte profile including magnesium and phosphates are important for rational measures taken for DM management. Patients with DM should be assessed for their serum electrolyte level, strict good glycaemic control, and reducing their alcohol consumption to reduce electrolyte imbalance and its complication.

Strengths and Limitations of the Study
Strength of the Study
In contrast to most of the previous studies, this study incorporated most biochemical liver function test parameters than any other previous study conducted, and the study tried to compare the prevalence of electrolyte imbalance between case and control groups.

Limitations of the Study

Despite the comparative cross-sectional nature of our study, it is challenging to demonstrate a cause-and-effect relationship.

Abbreviations

BMI, Body mass index; Ca^{+2}, Calcium; Cl^-, Chloride; DBP, Diastolic blood pressure; DM, Diabetes mellitus; FBS, Fasting blood sugar; IDF, International Diabetic Federation; K^+, Potassium; $Mg2^+$, Magnesium; Na^+, Sodium; $Po4^-$, Phosphate; ROMK, Renal outer medullary potassium channel; SBP, Systolic blood pressure; T2DM, Type 2 diabetes mellitus; TRPM6, Transient Receptor Potential Cation Channel Subfamily M Member 6; UoGCSH, University of Gondar Comprehensive Specialized Hospital.

Data Sharing Statement

Most of the data generated or analysed during this study are included in this published article. Additional files and full data will be available from the corresponding author upon a reasonable request.

Ethics Approval and Consent to Participate

Ethical clearance was obtained from the Research and Ethical Review Committee of the School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. Data collected only after full written informed consent was obtained.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests in this work.

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