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Original Article

Paediatrics Section

# Effect of Glycated Haemoglobin Deviations on Glomerular Filtration Rate and Electrolyte Homeostasis among Paediatric Patients with Type I Diabetes Mellitus

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## ABSTRACT

**Introduction:** Hyperglycaemia-induced electrolytic imbalance is a major contributing factor for the onset of complications observed in diabetes and other endocrine disorders. Children with Type I Diabetes Mellitus (T1DM) often exhibit electrolyte disturbances which contribute early onset of diabetic complications. Hyperglycaemia-induced electrolytic imbalance is a major contributing factor for the onset of complications observed in diabetes and other endocrine disorders.

**Aim:** To assess the effect of glycated haemoglobin deviations on estimated Glomerular Filtration Rate (eGFR) and electrolytes (sodium, potassium, calcium, and magnesium) in paediatric subjects with T1DM.

**Materials and Methods:** This retrospective study was conducted at King Abdullah Specialised Children's Hospital (KASCH)/ NGHA, Riyadh, Saudi Arabia, a tertiary care teaching hospital. Total 78 paediatric T1DM patients with diabetes for a duration of five years registered at the hospital for medical and nutritional care from January 2013 to December 2013, formed the study population. Data related to demography (age, gender, Body Mass Index [BMI]) and biochemical variables {Haemoglobin A1C (HbA1c), total cholesterol, Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Triglycerides (TG), urea, and serum creatinine, data related to electrolytes such as sodium, potassium, magnesium, calcium, and vitamin D} were extracted from the hospital information system. Frequencies, percentages, mean, standard deviation, student's t-test, tertiles with percentages, analysis of variance and Pearson correlation coefficient were used to analyse the data by statistical software Statistical Package for the Social Sciences (SPSS) (version 22.0).

**Results:** A total of 31 males and 47 females between ages 6-14 years were included in this study. eGFR (p-value=0.004) and sodium (p-value=0.013) were independently associated with HbA1c in T1DM even after adjusting the confounding factors such as age, BMI, and LDL. Whereas, other electrolytes (potassium, magnesium) and vitamin D showed an inverse relation with HbA1c but were not significant after adjusting for confounding factors (p-value <0.05). Serum creatinine (r-value=0.313, p-value=0.005) indicated a significant positive correlation with HbA1c while, eGFR (r-value=-0.344, p-value=0.002) and sodium (r-value=-0.236, p-value=0.040) showed a significant negative correlation with HbA1c.

**Conclusion:** Maintaining a balance between glycaemic control and nutritional therapy is essential to avoid the progressive development of diabetic complications in T1DM. In addition, early diagnosis, proper medications, including adequate insulin therapy and dietary supplements are needed to prevent diabetic complications.

**Keywords:** Hyperglycaemia, Juvenile, Osmolarity, Renal

## INTRODUCTION

Type I Diabetes Mellitus (T1DM) is an autoimmune disease characterised by insulin deficiency and hyperglycaemic conditions caused by the destruction of the pancreatic beta cells. The onset of T1DM usually happens in childhood, although it can present at any stage of life [1]. Globally, Saudi Arabia ranks the 5$^{th}$ in terms of incidence rates of T1DM (0-14 years) with 31.4 per 100,000 populations per year [1].

Electrolyte disorders due to kidney failure, dehydration, fever, and vomiting are common among patients with T1DM. In addition, malnutrition, gastrointestinal absorption capacity, acid-base abnormalities, and acute illness were leads electrolyte disturbances [2,3]. Hyperglycaemia-induced electrolytic imbalance is a major contributing factor for the onset of complications observed in diabetes and other endocrine disorders. Moreover, hyperglycaemia-induced osmotic fluid shifts or total-body fluid deficits due to osmotic diuresis cause a dilutional effect on electrolyte concentrations and cellular dehydration [4].

The osmotic diuresis can precipitate hypovolemic-hyponatremia. The presence of exogenous insulin favours hypokalemia by promoting the entry of Potassium ion ($K^+$) into skeletal muscles and hepatic cells by increasing the activity of the $Na^+$-$K^+$- ATPase pump. Moreover, hypokalemia may also be due to low intracellular magnesium ion ($Mg^{2+}$) concentration or hypomagnesemia. Hypomagnesemia activates the renal outer medullary $K^+$ channel to secrete more $K^+$ [5]. Inadequate dietary intake, glomerular hyper-filtration, altered insulin metabolism, diuretic administration, and recurrent metabolic acidosis are the causative factors for $Mg^{2+}$ imbalance for those with DM [6]. Vitamin D deficiency and hypoparathyroidism or hyperparathyroidism led to impaired calcium homeostasis in diabetic patients [5].

Circadian blood pressure changes among T1DM indicate the risk of renal function decline and hyperfiltration [7]. Proper diet and/or oral hypoglycaemic agents reduced Haemoglobin A1C (HbA1c) of those with T1DM nephropathy. Such reduction in HbA1c is associated with a significant decrease in Glomerular Filtration Rate (GFR) [8]. In addition, renal dysfunction is associated with poor glycaemic controlled T1DM [9].

Few studies have considered the consequences of variations in HbA1c on GFR and electrolyte homeostasis and none so far in paediatric subjects with T1DM among the Saudi population [10-12].

This study is a part of a previous retrospective cohort study with T1DM patients [13]. The present retrospective study aimed to investigate the association of HbA1c with electrolytes (sodium, potassium, calcium, and magnesium) and estimated Glomerular Filtration Rate (eGFR) of T1DM patients with five years of diabetes duration and examine the possible electrolytes involvement in glycaemic control of those with T1DM.

## MATERIALS AND METHODS

For the present retrospective study, a previous cohort study (IRB number: IRBC/834/16) conducted during 2016 [13] formed the data source. The data of patients with T1DM, who visited the hospital for a routine check-up between January 2009 and December 2013, from the hospital management information system (Best care) at King Abdullah Specialised Children's Hospital (KASCH), a tertiary care teaching hospital under the Ministry of National Guard Health Affairs (NGHA), Riyadh, Saudi Arabia, used for the previous [13] as well as for the present retrospective study.

The Institutional Review Board of King Abdullah International Medical Research Centre (KAIMRC) approved the study (IRB number: IRBC/834/16) and was conducted following the Declaration of Helsinki [14]. From a total of 164, T1DM patients included in the previous study, 78 patients with diabetes for a duration of five years were selected for this study following inclusion criteria [13]. Diagnosis of T1DM was done according to American Diabetes Association (ADA) criteria 2013 [15].

**Inclusion and Exclusion criteria:** The study inclusion criteria were Saudi nationals with TIDM of age between 6-14 years and affected with T1DM for five years. In addition, children with psychological and physical disabilities and other chronic diseases that may affect the growth pattern and patients with missing data were excluded from the study. Finally, a total of 78 patients were included in this study.

### Data Collection

Anthropometric and demographic variables such as age, gender, height, and weight were collected from hospital management information system. The Body Mass Index (BMI) was calculated using online calculator https://www.cdc.gov/healthyweight/bmi/calculator.html [16].

Biochemical data such as HbA1c, total cholesterol, Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), triglycerides, urea, and serum creatinine, data related to electrolytes such as sodium, potassium, magnesium, calcium, and vitamin D were also collected. In addition, the dietary pattern followed by the subjects was recorded.

For eGFR calculation, creatinine-based Bedside Schwartz equation (for children and adolescents 1-17 years) online calculator http://nephron.com/bedside_peds_nic.cgi was used [17].

## STATISTICAL ANALYSIS

Data analysis was done by using Statistical Package for the Social Sciences (SPSS) version 22.0. Frequencies and percentages were used to detail categorical variables whereas continuous variables were examined by the mean and standard deviation (mean±SD). Student's t-test compared data of male and female subjects. HbA1c tertiles were calculated using SPSS (version 22), with percentiles values (33.33 and 66.67) were generated by selecting cut points for three equals groups used for measuring the variability. The difference among and between groups was analysed by Analysis of Variance (ANOVA).

The Pearson correlation coefficient tested the correlations between individual variables. HbA1c was considered as dependent variable in multiple linear regression analysis, and electrolytes and eGFR as independent variables. The different combinations of confounding factors such as age, sex, BMI, and LDL were used to build several models to adjust. A p-value <0.05 was considered statistically significant.

## RESULTS

A total of 31 males and 47 females were included in this study. The demographic and biochemical characteristics of the study participants have been summarised in [Table/Fig-1] [16, 18-23]. The level of HbA1c showed that irrespective of gender, study participants had poor glycaemic control with values higher than normal. Male subjects had serum creatinine values (65.77±14.74 µmol/L), whereas female subjects showed eGFR values (91.47±12.62 mL/min/1.73m$^2$). Both males and females exhibited lower vitamin D levels. The majority (78.21%) of the male and female subjects followed American Diabetes Association (ADA) recommended diet. A comparison between male and female showed significant differences between triglycerides (p-value=0.030), serum creatinine (p-value=0.015), urea (p-value=0.001) and eGFR (p-value=0.002).

| Parameters | Male | Female | Normal range | p-value |
|---|---|---|---|---|
| Patients | 31 (39.7) | 47 (60.3) | NA | NA |
| Age(years)* | 10.65±2.52 | 11.40±1.85 | NA | 0.130 |
| Age ≤10 (years) n (%) | 12 (38.7) | 15 (31.9) | NA | NA |
| Age >10 (years) n (%) | 19 (61.3) | 32 (68.1) | NA | NA |
| BMI (kg/m$^2$)** | 18.48±4.04 | 20.11±4.38 | 18.5-24.9 [16] | 0.102 |
| HbA1c (%)** | 10.67±1.43 | 10.53±1.77 | ≤6.5 [18] | 0.721 |
| Total cholesterol (mmol/L)** | 5.16±0.70 | 4.51±0.72 | <4.4 [19] | 0.112 |
| LDL (mmol/L)** | 2.41±0.90 | 2.23±0.69 | <2.8 [19] | 0.673 |
| HDL (mmol/L)** | 1.47±0.12 | 1.41±0.21 | >1.2 [19] | 0.576 |
| Triglycerides (mmol/L)** | 0.97±0.10 | 0.72±0.19 | <1.0 [19] | 0.030*** |
| Urea (mmol/L)** | 4.84±1.29 | 3.93±1.05 | 2.5-6.5 [20] | 0.001*** |
| Serum creatinine (µmol/L)** | 65.77±14.74 | 58.98±9.47 | 25-83 [20] | 0.015*** |
| eGFR (mL/min/1.73 m$^2$)** | 81.39±14.52 | 91.47±12.62 | ≥90 [21] | 0.002*** |
| Sodium (mEq/L)** | 134.53±2.75 | 135.52±3.35 | 136-145 [22] | 0.183 |
| Potassium (mEq/L)** | 4.32±0.499 | 4.23±0.38 | 3.5-5.5 [22] | 0.398 |
| Calcium (mmol/L)** | 2.40±0.138 | 2.37±0.115 | 2.2-2.67 [22] | 0.361 |
| Magnesium (mmol/L)** | 0.768±0.078 | 0.742±0.075 | 0.66-0.94 [22] | 0.183 |
| Vitamin D (nmol/L)** | 36.90±13.74 | 39.59±19.22 | >50 [23] | 0.655 |
| **Dietary pattern** | | | | |
| Regular diet n (%) | 6 (35.3) | 11 (64.7) | NA | |
| ADA recommended diet n (%) | 25 (41) | 36 (59) | NA | |

**[Table/Fig-1]:** Demographic and clinical characteristics of paediatrics with type 1 diabetes (n=78).
NA: Not applicable; BMI: Body mass index; LDL: Low density lipoprotein; HDL: High-density lipoprotein; eGFR: Estimated glomerular filtration rate; ADA: American diabetes association
*Numbers in parenthesis indicate percentage, **Data were presented as mean±SD, ***p<0.05 was considered as significant (Students t-test)

[Table/Fig-2] showed the classification of clinical and biochemical parameters of children with T1DM based on HbA1c tertiles (tertile 1, <9.7; tertile 2, 9.7-11.1; tertile 3, >11.1). The mean age, triglycerides, eGFR, sodium, and vitamin D were higher among HbA1c tertile 1. In contrast, LDL, urea, serum creatinine, and magnesium were higher among HbA1c tertile 3. Across the tertiles of HbA1c, there was significant difference in HDL (p-value=0.003), serum creatinine (p-value=0.045) and eGFR (p-value=0.017).

[Table/Fig-3] illustrated the results of the Pearson correlation analysis of HbA1c levels with biochemical parameters and electrolytes. The results indicated that age, BMI, triglycerides, LDL, urea, and calcium were shown an inverse relation with HbA1c but not significant. Serum creatinine (r-value=0.313, p-value=0.005) indicated a significant positive correlation with HbA1c while, eGFR (r-value=-0.344, p-value=0.002) and sodium (r-value=-0.236, p-value=0.040) showed a significant negative correlation with HbA1c.

| Parameters | HbA1c <9.7% (Mean±SD) (n=25) | HbA1c=9.7-11.1% (Mean±SD) (n=28) | HbA1c >11.1% (Mean±SD) (n=25) | p-value |
|---|---|---|---|---|
| Age (years) | 11.48±1.91 | 10.96±2.20 | 10.88±2.36 | 0.571 |
| BMI (kg/m$^2$) | 19.91±4.34 | 20.45±4.60 | 17.92±3.58 | 0.084 |
| Total cholesterol (mmol/L) | 4.13±0.46 | 4.99±0.75 | 4.67±0.84 | 0.176 |
| LDL (mmol/L) | 2.36±0.44 | 2.11±0.77 | 2.48±1.00 | 0.701 |
| HDL (mmol/L) | 1.24±0.14 | 1.56±0.14 | 1.37±0.13 | 0.003* |
| Triglycerides (mmol/L) | 0.84±0.24 | 0.77±0.23 | 0.73±0.07 | 0.742 |
| Urea (mmol/L) | 4.31±1.09 | 4.23±1.34 | 4.35±1.27 | 0.937 |
| Serum creatinine (µmol/L) | 56.92±6.36 | 62.75±15.02 | 65.24±12.13 | 0.045* |
| eGFR (mL/min/1.73m$^2$) | 93.03±11.06 | 87.60±13.11 | 81.74±16.30 | 0.017* |
| Sodium (mEq/L) | 136.0±2.64 | 135.08±2.95 | 134.32±3.67 | 0.169 |
| Potassium (mEq/L) | 4.22±0.422 | 4.29±0.52 | 4.27±0.34 | 0.813 |
| Calcium (mmol/L) | 2.35±0.11 | 2.42±0.13 | 2.36±0.11 | 0.264 |
| Magnesium (mmol/L) | 0.73±0.09 | 0.75±0.08 | 0.76±0.06 | 0.537 |
| Vitamin D (nmol/L) | 41.39±23.20 | 36.80±14.86 | 38.18±12.43 | 0.773 |

**[Table/Fig-2]:** Classification of clinical and biochemical parameters of paediatrics with Type 1 Diabetes as per HbA1c tertiles.
*p-value <0.05 was considered as significant compared to HbA1c (One-way ANOVA)

| Parameters | r | p-value |
|---|---|---|
| Age (years) | -0.019 | 0.870 |
| BMI (kg/m$^2$) | -0.101 | 0.381 |
| Total cholesterol (mmol/L) | 0.248 | 0.354 |
| LDL (mmol/L) | -0.038 | 0.885 |
| HDL (mmol/L) | 0.318 | 0.214 |
| Triglycerides (mmol/L) | -0.225 | 0.419 |
| Urea (mmol/L) | -0.001 | 0.993 |
| Serum creatinine (µmol/L) | 0.313 | 0.005* |
| eGFR (mL/min/1.73m$^2$) | -0.344 | 0.002* |
| Sodium (mEq/L) | -0.236 | 0.040* |
| Potassium (mEq/L) | 0.111 | 0.340 |
| Calcium (mmol/L) | -0.010 | 0.949 |
| Magnesium (mmol/L) | 0.008 | 0.958 |
| Vitamin D (nmol/L) | 0.002 | 0.989 |

**[Table/Fig-3]:** Relationship between clinical and biochemical parameters with HbA1c levels of paediatrics with Type 1 Diabetes.
*p-value <0.05 was considered as significant

Multiple linear regression analysis of electrolytes and eGFR with HbA1c as dependent variable were shown in [Table/Fig-4]. The eGFR (p-value=0.004) showed an inverse association with HbA1c after adjusting for age, sex, BMI, and LDL. Furthermore, an inverse association of sodium and HbA1c was found after adjusting for confounding factors such as age, sex, BMI, and LDL. Additionally, other electrolytes (potassium, magnesium) and vitamin D were also showed an inverse relation with HbA1c but no longer significant after adjusting for age, sex, BMI, and LDL.

| Parameters | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| | Standard β | p-value | Standard β | p-value | Standard β | p-value | Standard β | p-value |
| eGFR | -0.596 | 0.012* | -0.596 | 0.019* | -0.651 | 0.004* | -0.673 | 0.004* |
| Sodium | -0.626 | 0.012* | -0.664 | 0.012* | -0.618 | 0.013* | -0.645 | 0.013* |
| Potassium | -0.169 | 0.548 | -0.071 | 0.827 | -0.046 | 0.881 | -0.107 | 0.761 |
| Calcium | 0.457 | 0.216 | 0.514 | 0.256 | 0.473 | 0.339 | 0.501 | 0.105 |
| Magnesium | -0.252 | 0.454 | -0.413 | 0.385 | -0.143 | 0.769 | -0.155 | 0.758 |
| Vitamin D | -0.271 | 0.449 | -0.286 | 0.510 | -0.341 | 0.446 | -0.277 | 0.563 |

**[Table/Fig-4]:** Regression analysis of different clinical and biochemical parameters with HbA1c as dependent variable.
Model 1, crude. Model 2, adjusted for age and sex, Model 3, adjusted for age, sex, and BMI. Model 4, adjusted for age, sex, BMI and LDL; *p< 0.05 were considered as significant

## DISCUSSION

Even with significant medical and technological progress, the control and management of T1DM continues to be suboptimal. The utmost challenge encompasses the difficulty in regulating hyperglycaemia, which is a major causative factor for elevated HbA1c [24]. Despite ADA diet, subjects had poor glycaemic control. It was observed that the male subjects had shown elevated serum creatinine levels, and the creatinine levels of both genders were significantly different. Molitoris BA reported that females usually have lower creatinine levels than males because of less muscle mass [25]. eGFR aids in the early identification of diabetic nephropathy [26]. The eGFR was significantly different among male and female T1DM subjects. The mean eGFR of male subjects (81.39±14.52 mL/min/1.73 m$^2$) was significantly lower than that of female subjects (91.47±12.62 mL/min/1.73 m$^2$). The lower eGFR level in males indicates the mild loss of kidney function [27]. A previous follow-up study reported that hyperfiltration was prevalent in adolescents with T1DM and was associated with rapid GFR decline [7].

Classification of HDL based on HbA1c showed an ascending trend in tertile 2 and then a descending tendency. The HDL values were significantly different (p-value=0.003) across the tertiles. A similar but insignificant trend was observed for total cholesterol based on HbA1c. Pérez A et al., reported that among poorly controlled T1DM patients, low HDL is the common dyslipidemia disorder [28]. In this study, urea levels were significantly higher among male patients than female subjects (p-value=0.001). Amartey NA et al., reported a similar finding among patients with type 2 diabetes [29]. The serum urea levels of T1DM did not differ among tertiles of HbA1c. In previous studies, no difference was found in serum urea levels in T1DM with diabetes duration of 12.2±5.8 years and elderly T1DM patients compared with control subjects [30,31]. Serum creatinine (p-value=0.045) and eGFR (p-value=0.017) based on tertiles of HbA1c were significantly different across the tertiles. Serum creatinine values showed an increasing trend, whereas the eGFR values presented a decreasing trend from tertile 1 to 3. A five-year follow-up study observed that reduced eGFR was observed in 4.3% of the subjects and a long history of T1DM with poor glycaemic control doubles the risk of reduced GFR [32].

In this study, age showed an inverse but non significant relation with HbA1c. Increased treatment barriers have been reported among children of 5 to 7 years of age [33]. The BMI indicated an inverse relationship with HbA1c in the study. In general, obesity is more in the 1-6 years age group among the Saudi population. However, a significant decrease in the incidence rate of obesity among 12-18-year-old boys and girls was identified [34]. The majority of the study participants were above 10-year-old. In addition, increased insulin administered to improve glycaemic control may contribute to increase BMI in youth with T1DM [35].

A non-significant inverse relation between LDL or triglycerides levels with HbA1c was found among the study subjects. Homma TK et al., observed no correlation between poor glycaemic control and HDL, LDL, total cholesterol or the triglycerides levels in T1DM [36]. According to Alves C et al., dyslipidaemia is most likely to be found in newly diagnosed individuals with diabetes mellitus, those who are metabolically decompensated, or patients experiencing diabetic ketoacidosis [37].

Likewise, electrolyte disturbances are well-known consequences of the diabetic pathology associated with hyperglycaemia [5]. The study results indicated that serum concentrations of sodium decreased with an increase in HbA1c levels in patients with T1DM. In addition, Caduff A et al., showed that plasma concentrations of $Na^+$ decrease in response to moderate hyperglycaemia in patients with T1DM [38]. The mechanism of hyperglycaemia-induced hyponatremia has gained wider acceptance since the increased osmolarity associated with elevated plasma glucose levels leads to an osmotically driven flux of water from cells into the interstitium blood, thus effectively diluting the ions in the blood [39,40].

The causes of hypokalemia in people with diabetes include gastrointestinal loss of $K^+$ due to malabsorption syndromes, renal loss, other electrolyte disorders, etc. In addition, insulin administration can induce hypokalemia because it promotes the entry of $K^+$ into skeletal muscles and hepatic cells by increasing the activity of the $Na^+$-$K^+$ ATPase pump [5]. An insignificant inverse relationship between potassium and HbA1c levels was observed in our study. Hasona NA and Elasbali A showed a reduction in serum $Na^+$ and $K^+$ levels in T1DM [41].

A long-term abnormal carbohydrate metabolism leads to an inverse relation between vitamin D and HbA1c in T1DM. It is associated with hypovitaminosis D. Poor glycaemic control may affect directly on vitamin D metabolism and activity [42], and/or vitamin D has an indirect role via regulation of calcium homeostasis in various mechanisms (like pancreatic beta-cell dysfunction, impaired insulin action, and systemic inflammation) related to the pathophysiology of T1DM [43]. Yassin MM et al., reported a significant inverse association was found between HbA1c and vitamin D; conversely, a significant positive correlation was found with calcium levels in T1DM with 9.1±7.0 years of diabetes duration [44]. Meanwhile, the study participants also showed a similar trend of HbA1c with vitamin D and calcium levels but those were non-significant; this might be due to the shorter diabetes duration (five years) among our study participants.

In general, uncontrolled hyperglycaemia may increase magnesium excretion through osmotic diuresis, leading to a vicious circle [45]. Insulin deficiency may explain the increased urinary magnesium excretion because insulin has been recognised to stimulate magnesium conservation in the loop of Henle and distal tubule [46]. Moreover, hypomagnesemia in T1DM often co-exists with other electrolyte disorders such as hyponatremia and hypocalcaemia [5]. Asmaa MN et al., reported a significant negative correlation between serum magnesium and HbA1c levels [47]. In contrast, in this study, a weak positive correlation was shown between magnesium and HbA1c levels, which might be due to the low sample size and shorter duration of diabetes.

In the present study, eGFR and sodium were significantly associated with HbA1c in T1DM even after adjusting the confounding factors such as age, sex, BMI, and LDL. The other electrolytes (potassium, magnesium) and vitamin D also showed an inverse relation with HbA1c but were no longer significant after adjusting for age, BMI and LDL. The induction of oxidative stress, secretion of inflammatory cytokines, and endothelial damage was associated with variability in blood glucose levels. These modifications may contribute to the pathogenesis of diabetic complications [48,49]. Similarly, in kidneys, homeostatic variations may also be detrimental and induce the secretion of growth factors such as Insulin-like Growth Factor-1 (IGF-1) and Vascular Endothelial Growth Factor (VEGF) [50,51]. An excessive glycaemic variability on the other hand, may indicate poor treatment adherence and self-management patient compliance, decreased quality of life, lack of social support, and frequent infective complications [52]. HbA1c variability was associated with renal function deterioration in T1DM with multi-ethnic background [53]. The current study demonstrated that HbA1c is inversely associated with eGFR after being adjusted for confounding factors.

### Limitation(s)

The study's primary limitations were related to data collection from the electronic files from the best care system. Due to the unavailability of data related to insulin dosage, authors did not consider the effect of insulin therapy on electrolytes. This study cannot correctly illustrate the root cause of electrolyte imbalance in T1DM due to the unavailability of data related to insulin dosage, fasting blood glucose, intake of dietary supplements. The study participants have a similar duration of diabetes, the cross-sectional study design, unavailability of confounding factor (blood pressure) and the low sample size limit from evaluating the mechanistic role of hyperglycaemia with electrolytes in the progression of diabetes. This study could not evaluate the influence of diet on serum electrolyte level due to the unavailability of data on daily dietary intake.

## CONCLUSION(S)

An inverse association between HbA1c and eGFR and the electrolyte sodium were observed among T1DM patients with diabetes for a duration of five years. In future, these findings might have great potential as a management tool for diabetes in clinical practice. Therefore, maintaining a balance between glycaemic control through nutritional therapy is essential to avoid early development of complications in T1DM. In addition, early diagnosis, and proper medications, including adequate insulin therapy and dietary supplements are needed to prevent the complications related to diabetes.

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