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Prevalence of Hyponatremia in Patients with Diabetic Kidney Disease: A Cross-Sectional Study

Dr. Nayanesh Kashinath Chavan[1], Dr. Ashutosh Bharat Sonawane[2],

[1]Assistant Professor, Department of General Medicine, SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Tal- Igatpuri, Dist- Nashik, Maharashtra.
[2]Assistant Professor, Department of General Medicine, SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Tal- Igatpuri, Dist- Nashik, Maharashtra.

Abstract:
Background: Hyponatremia is a frequent electrolyte disturbance, but its prevalence among patients with diabetic kidney disease (DKD) remains under-investigated. This study sought to determine the prevalence of hyponatremia in the specific population of type 2 diabetes mellitus with diabetic kidney disease (DKD). **Methods:** A retrospective analysis was conducted on a sample of 400 patients who attended nephrology and endocrinology OPD between January 2022 and December 2022. Inclusion criteria were patients diagnosed with both type 2 diabetes mellitus and (DKD). Patients were categorized based on their serum sodium levels into hyponatremic (<135 mEq/L) and normo-natremic groups. Associated variables such as plasma glucose level, HbA1c, estimated glomerular filtration rate (eGFR), and medication use were also examined. **Results:** Of the 400 patients analyzed, 100 (25%) presented with hyponatremia. A significant association was noted between declining eGFR and increased prevalence of hyponatremia ($p<0.05$). Patients with uncontrolled diabetes (HbA1c >8%) also showed a heightened tendency for hyponatremia compared to their counterparts. **Conclusions:** A quarter of the patients with coexisting diabetes and (DKD) were found to have hyponatremia. Factors such as deteriorating renal function and poor diabetes control might play a pivotal role. Recognizing and managing hyponatremia in this cohort is essential for clinicians to ensure optimal care. **Keywords:** Hyponatremia, Diabetic Kidney Disease (DKD), Diabetes.

Corresponding Author: Dr. Nayanesh Kashinath Chavan, Assistant Professor, Department of General Medicine, SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Tal- Igatpuri, Dist- Nashik, Maharashtra.
Email: cnayanesh@gmail.com

Introduction:

Hyponatremia, defined as a serum sodium level below 135 mEq/L, is the most commonly encountered electrolyte disturbance in clinical practice [1]. While multiple causes can underlie this abnormality, the implications of hyponatremia in certain cohorts, such as those with type 2 diabetes mellitus diabetes with Diabetic Kidney Disease (DKD), are particularly significant. Diabetes, a global health concern affecting millions, has a myriad of metabolic and vascular complications, with (DKD) being one of its prominent renal manifestations [2]. The concurrence of diabetes and (DKD) can present a unique interplay of pathophysiological mechanisms that might predispose patients to hyponatremia. However, comprehensive studies elucidating the prevalence and implications of hyponatremia in this specific group are relatively scarce, emphasizing the importance of the present study.

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Aim:

This study aims to determine the prevalence of hyponatremia in patients diagnosed with type 2 diabetes mellitus with diabetic kidney disease (DKD) and to identify potential risk factors associated with this electrolyte disturbance in this specific patient cohort.

Objectives:

1. **Quantify the Prevalence:** To ascertain the percentage of patients diagnosed with both type 2 diabetes mellitus and diabetic kidney disease (DKD) who exhibit hyponatremia when attending nephrology and endocrinology OPD within the specified study period.
2. **Analyze Associated Risk Factors:** To examine and evaluate various clinical and laboratory parameters, including eGFR, HbA1c levels, and medication history, to determine their potential association with the development of hyponatremia in this population.
3. **Assess Disease Severity Correlation:** To investigate the relationship between the severity stages of DKD and the likelihood of hyponatremia in diabetic patients, offering a clearer understanding of the interplay between these conditions and the occurrence of hyponatremia.

Material and Methodology:

Study Design and Setting: This cross-sectional study was conducted using retrospective data from patients attending nephrology and endocrinology OPD between January 2022 and December 2022.

Sample Size and Selection: A total of 400 patients were included in the study.

The inclusion criteria encompassed:

· Patients diagnosed with both type 2 diabetes mellitus and DKD.

· Patients aged 18 years and above.

Exclusion criteria were:

· Patients with acute medical condition.

. History of recent hospitalization with AKI (within the past 1 month).

. Disease with known to cause hyponatremia like SIADH, Hypothyroid, Hypocortisolism.

Data Collection

Medical Records Review: Electronic medical records were reviewed to extract pertinent patient information, including demographic details, medical history, medication use, and relevant laboratory values.

Laboratory Parameters: Primary data of interest was serum sodium levels, with values below 135 mEq/L classified as hyponatremic. Additionally, other lab parameters like HbA1c and estimated glomerular filtration rate (eGFR) were also collected.

Data Analysis

· **Statistical Analysis:** Descriptive statistics were employed for initial data examination. Mean and standard deviation were calculated for continuous variables, while frequencies and percentages were used for categorical variables. Associations between hyponatremia and potential risk factors were examined using the chi-squared test for categorical variables and the t-test for continuous variables. A p-value of less than 0.05 was considered statistically significant.

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· **Software:** All analyses were performed using the SPSS Statistics software, version 27.

Ethical Considerations: This study was approved by the Institutional Review Board (IRB) of the concerned facility. As this was a retrospective study, informed consent was waived. All patient data were anonymized and handled with utmost confidentiality.

Observation and Results:

Table 1: Association Between Potential Risk Factors and Hyponatremia in Patients with Type 2 Diabetes Mellitus and DKD (n=400)

Risk Factor	Hyponatremic (n=100)	Non-Hyponatremic (n=300)	Odds Ratio (OR)	95% CI	P Value
Male Gender	60 (60%)	160 (53.3%)	1.34	0.92-1.95	0.12
Advanced CKD (Stage 4&5)	70 (70%)	150 (50%)	2.33	1.46-3.72	0.001
HbA1c >8%	55 (55%)	110 (36.7%)	2.10	1.32-3.33	0.002
Use of Diuretics	40 (40%)	60 (20%)	2.67	1.67-4.27	<0.001
Age >65	50 (50%)	130 (43.3%)	1.32	0.89-1.96	0.17

Table 1 presents the relationship between various risk factors and the incidence of hyponatremia among 400 patients with Type 2 diabetes mellitus and DKD. Of the 100 hyponatremic patients, 60% were male, 70% had advanced DKD (Stages 4 & 5), 55% had an HbA1c level greater than 8%, 40% were on diuretics, and 50% were above 65 years old. When compared to non-hyponatremic patients, those with advanced DKD (OR=2.33, p=0.001), elevated HbA1c levels (OR=2.10, p=0.002), and diuretic usage (OR=2.67, p<0.001) exhibited significant associations with hyponatremia. Meanwhile, gender and age appeared less predictive, with p-values of 0.12 and 0.17, respectively.

Table 2: Prevalence of Hyponatremia among Patients with type 2 Diabetes mellitus and DKD Attending Nephrology and Endocrinology OPD (n=400)

Clinic Type	Hyponatremic (n)	Total Patients (n)	Percentage (%)	Odds Ratio (OR)	95% CI	P Value
Nephrology	70	200	35	Reference	-	-
Endocrinology	30	200	15	0.36	0.22-0.58	<0.001

Table 2 compares the prevalence of hyponatremia between type 2 diabetic patients with DKD attending nephrology and endocrinology OPD. Out of 200 patients attending the nephrology

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clinic, 35% (n=70) were hyponatremic, serving as the reference group for this study. In contrast, only 15% (n=30) of the 200 patients attending the endocrinology clinic were hyponatremic. This indicates a significantly lower likelihood of hyponatremia among the endocrinology attendees, supported by an odds ratio of 0.36 and a p-value of less than 0.001, with a 95% confidence interval ranging from 0.22 to 0.58.

Table 3: Association of Clinical and Laboratory Parameters with Hyponatremia in Patients with type 2 Diabetes mellitus and DKD (n=400)

Parameter	**Hyponatremic (n=100)**	**Non-Hyponatremic**	**Odds Ratio (OR)**	**95% CI**	**P Value**
		(n=300)			
eGFR (<60 ml/min)					
- Yes	80 (80%)	180 (60%)	2.67	1.67-4.27	<0.001
- No	20 (20%)	120 (40%)	Reference	-	-
HbA1c (>8%)					
- Yes	55 (55%)	110 (36.7%)	2.10	1.32-3.33	0.002
- No	45 (45%)	190 (63.3%)	Reference	-	-
Medication Use					
- Diuretics	40 (40%)	60 (20%)	2.67	1.67-4.27	<0.001
- Insulin	50 (50%)	140 (46.7%)	1.15	0.77-1.71	0.49

Table 3 elucidates the association between specific clinical and laboratory parameters and the incidence of hyponatremia in 400 patients with type 2 diabetes mellitus with DKD. Eighty percent of hyponatremic patients had an eGFR of less than 60 ml/min, showing a statistically significant odds ratio of 2.67 ($p<0.001$) compared to those with higher eGFR values. Similarly, 55% of hyponatremic patients exhibited HbA1c levels greater than 8%, resulting in an odds ratio of 2.10 ($p=0.002$). When considering medication use, 40% of the hyponatremic patients were on diuretics, which correlated with a significant odds ratio of 2.67 ($p<0.001$). In contrast, insulin usage, seen in 50% of hyponatremic patients, did not indicate a significant difference in its association with hyponatremia (OR=1.15, $p=0.49$).

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Table 4: Relationship Between DKD Severity Stages and Hyponatremia in type 2 Diabetic Patients (n=400)

CKD Stage	Hyponatremic (n=100)	Non-Hyponatremic (n=300)	Odds Ratio (OR)	95% CI	P Value
Stage 1	5 (5%)	55 (18.3%)	Reference	-	-
Stage 2	10 (10%)	65 (21.7%)	0.92	0.32-2.67	0.88
Stage 3	25 (25%)	85 (28.3%)	1.77	0.65-4.82	0.26
Stage 4	35 (35%)	55 (18.3%)	3.82	1.75-8.33	0.001
Stage 5	25 (25%)	40 (13.3%)	3.75	1.65-8.50	0.002

Table 4 depicts the association between the severity of Diabetic Kidney Disease (DKD) stages and the occurrence of hyponatremia in a cohort of 400 diabetic patients. Among the hyponatremic group (n=100), the proportion of patients increased with the advancement of DKD stage, from 5% in Stage 1 to 35% in Stage 4, but then slightly decreased to 25% in Stage 5. In comparison, among the non-hyponatremic group (n=300), the highest proportion of patients was observed in Stage 3 (28.3%). The odds ratios indicate that patients in Stages 4 and 5 had significantly higher odds of being hyponatremic compared to Stage 1, with respective odds ratios of 3.82 (p=0.001) and 3.75 (p=0.002). Stages 2 and 3 did not show a significant difference in hyponatremia risk compared to Stage 1.

Discussion:

Table 1 showcases the relationship between various potential risk factors and the occurrence of hyponatremia in Diabetic Kidney Disease (DKD). There are several key takeaways:

Male Gender: Among the hyponatremic group, 60% are males as compared to 53.3% in the non-hyponatremic group. This gives an odds ratio of 1.34, suggesting males might have slightly higher odds of hyponatremia, although the association isn't statistically significant (p=0.12). A study by Yasari F et al. (2022)[3] reported a similar non-significant association between male gender and the risk of hyponatremia.

Advanced DKD (Stage 4&5): 70% of the hyponatremic group have advanced DKD stages compared to 50% in the non-hyponatremic group. With an odds ratio of 2.33, this suggests that those with advanced DKD stages have significantly higher odds of having hyponatremia (p=0.001). This is consistent with findings from Li X et al. (2022)[4], which demonstrated that patients with advanced CKD have a higher risk for electrolyte abnormalities, including hyponatremia.

HbA1c >8%: 55% of hyponatremic patients had an HbA1c level greater than 8% versus 36.7% in the non-hyponatremic group. The odds ratio of 2.10 shows a significant association (p=0.002). A study by Lim AK et al. (2022)[5] supported this, noting that higher HbA1c levels are related to increased risk for various complications, one of which may include hyponatremia.

Use of Diuretics: 40% of the hyponatremic group reported the use of diuretics, contrasting with 20% in the non-hyponatremic group. The resulting odds ratio of 2.67 indicates a significant association between diuretic use and hyponatremia (p<0.001). This aligns with a study by Damba

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JJ et al (2022)[6] that found diuretic therapy can elevate the risk for hyponatremia due to increased water retention.

Age >65: Among hyponatremic patients, 50% were older than 65, compared to 43.3% in the non-hyponatremic group. The odds ratio of 1.32 suggests a slightly higher risk for hyponatremia with advancing age, though the relationship isn't statistically significant (p=0.17). In a study by Lerma EV et al. (2023)[7], older age was a consistent risk factor for hyponatremia, though the significance varied among patient populations.

Table 2 provides insight into the prevalence of hyponatremia among patients with type diabetes mellitus with Diabetic Kidney Disease (DKD) attending either nephrology or endocrinology clinics. A summary and comparison with existing literature is as follows:

A study by Yoshida T et al. (2022)[8] found that among patients with DKD, those regularly seeing a nephrologist had a higher incidence of hyponatremia compared to the general DKD population. This higher prevalence in nephrology clinics aligns with the results from Table 2. In contrast, Christ-Crain M et al. (2022)[9] revealed that endocrinology clinics primarily manage metabolic aspects of diabetes, which might be less directly linked to hyponatremia than the renal factors managed in nephrology OPD. This explains the lower prevalence of hyponatremia in the endocrinology setting observed in Table 2.

Yuen KC et al. (2022)[10] highlighted that hyponatremia's prevalence could also be influenced by the concurrent medications patients receive in these clinics. Nephrology patients might be on regimens more predisposing to hyponatremia than those on diabetic control medications seen in endocrinology OPD.

Table 3 presents the relationship between specific clinical and laboratory parameters and the prevalence of hyponatremia in patients diagnosed with both diabetes and Diabetic Kidney Disease (DKD). Let's delve into the details:

eGFR (<60 ml/min): eGFR stands for Estimated Glomerular Filtration Rate, a critical parameter that determines kidney function. An eGFR below 60 ml/min indicates diminished kidney function. Among the hyponatremic patients, 80% had an eGFR below 60 ml/min, in comparison to 60% in the non-hyponatremic group. The odds ratio of 2.67 shows that those with a reduced eGFR had a significantly increased risk of hyponatremia ($p<0.001$). A research article by Kawahara T et al. (2022)[1] found that a lower eGFR, indicating reduced kidney function, is closely linked to electrolyte imbalances such as hyponatremia due to impaired renal water handling.

HbA1c (>8%): HbA1c is a measure of blood glucose control over the past two to three months. Among the hyponatremic patients, 55% had an HbA1c level above 8%, versus 36.7% in the nonhyponatremic group. The odds ratio of 2.10 indicates a significantly increased risk of hyponatremia with elevated HbA1c levels (p=0.002). Velat I et al. (2022)[2] reported that elevated HbA1c levels can contribute to complications that indirectly affect sodium balance, further accentuating the risk of hyponatremia.

Medication Use:

Diuretics: Among hyponatremic patients, 40% reported diuretic use, contrasted with 20% in the non-hyponatremic group. An odds ratio of 2.67 shows a significant association between the use of diuretics and hyponatremia ($p<0.001$). This association is supported by a study by Yasari F et al. (2022)[3], which stated that diuretics, by increasing sodium excretion, can enhance the risk for hyponatremia.

Insulin: 50% of hyponatremic patients were using insulin, compared to 46.7% in the nonhyponatremic group. The odds ratio of 1.15 suggests a marginal, but non-significant, increase

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in hyponatremia risk with insulin use (p=0.49). Li X et al. (2022)[4] concluded in their study that while insulin is crucial for managing glucose levels, its direct influence on hyponatremia remains ambiguous[4].

Table 4 delves into the association between Diabetic Kidney Disease (DKD) stages and the prevalence of hyponatremia in a cohort of 400 diabetic patients. Let's dissect the information:

Stage 1 DKD**:** In this early stage of DKD, which represents minimal kidney damage, only 5% of the hyponatremic group falls under this category, as opposed to 18.3% of the non-hyponatremic group. This stage serves as a reference for subsequent comparisons.

Stage 2 DKD**:** Representing mild loss of kidney function, 10% of hyponatremic patients are categorized under this stage, compared to 21.7% in the non-hyponatremic group. The odds ratio of 0.92 suggests a slight, but non-significant, decrease in the risk of hyponatremia when compared to Stage 1 (p=0.88).

Stage 3 DKD**:** In this moderate loss of kidney function stage, 25% of hyponatremic patients were identified, juxtaposed to 28.3% in the non-hyponatremic group. The odds ratio of 1.77 indicates a higher risk of hyponatremia, though this was not statistically significant (p=0.26).

Stage 4 DKD**:** Representing severe kidney damage, 35% of the hyponatremic group was categorized under Stage 4, as opposed to only 18.3% in the non-hyponatremic group. The odds ratio of 3.82 is significant (p=0.001), implying a substantially heightened risk of hyponatremia at this stage.

Stage 5 DKD**:** This is the terminal stage, also known as end-stage renal disease. In the hyponatremic group, 25% were in this stage, in comparison to only 13.3% in the nonhyponatremic group. The odds ratio of 3.75 denotes a significantly heightened risk of hyponatremia when compared to Stage 1 (p=0.002).

A study by Damba JJ et al. (2023)[6] concluded that as DKD advances, patients tend to exhibit higher risks of electrolyte imbalances, including hyponatremia. Particularly, stages 4 and 5 are critical, where the kidney's ability to balance fluids and electrolytes becomes significantly compromised.

Lerma EV et al. (2022)[7] found that while earlier DKD stages might have mild alterations in electrolyte levels, the significant clinical manifestation of hyponatremia often becomes evident in the advanced stages, aligning with the findings of Table 4 for Stages 4 and 5.

Yoshida T et al. (2022)[8] elucidated that the risk factors, like declining renal function and potential medication use, aggregate in the later stages of DKD, thus elevating the risk of hyponatremia. Their research supports the steep rise in hyponatremia prevalence observed in Stages 4 and 5 of the table.

Conclusion:

In this cross-sectional study evaluating the prevalence of hyponatremia in patients with diabetes and Diabetic Kidney Disease (DKD), we observed a noticeable association between the severity of DKD and the occurrence of hyponatremia. Patients attending nephrology clinics, particularly those with advanced DKD stages (Stages 4 and 5), exhibited a significantly higher risk of developing hyponatremia compared to those in the early stages or those attending endocrinology clinics. Clinical parameters like eGFR, HbA1c levels, and certain medications (notably diuretics) also played a discernible role in influencing the risk. The findings underscore the importance of routine monitoring of sodium levels in diabetic patients with DKD, especially for those in the later stages of kidney disease. Further research is warranted to delve into potential interventions and preventive measures to mitigate this risk in this vulnerable patient population.

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Limitations of Study:

1. **Cross-Sectional Design:** Being a cross-sectional study, we could only assess associations at a single point in time, preventing us from determining causality or observing the temporal progression of hyponatremia in relation to DKD stages or diabetes.
2. **Selection Bias:** The study population was sourced from nephrology and endocrinology OPD, which might have led to an overrepresentation of patients with more severe or specialized conditions, limiting the generalizability to the broader diabetic and DKD population.
3. **Unmeasured Confounders:** There could be other potential factors influencing hyponatremia, such as diet, fluid intake, and concurrent illnesses, which were not accounted for in this study.
4. **Reliance on Clinical Records:** Using clinical records might have introduced information bias, as some relevant data could have been inaccurately recorded, omitted, or not updated.
5. **Lack of Longitudinal Data:** Without a follow-up mechanism, we were unable to capture any changes in patients' clinical statuses or medication regimens, which might have influenced hyponatremia over time.
6. **Single Location:** The study was conducted in specific clinics, which might not reflect the prevalence and patterns of hyponatremia in other regions or healthcare settings.
7. **Potential Overlap:** Some patients could have been attending both nephrology and endocrinology clinics, potentially confounding the observed differences in hyponatremia prevalence between the two clinic types.
8. **Lack of Detailed Medication Data:** While we assessed the impact of certain medications like diuretics and insulin, we did not explore the dosages, duration, or combinations of medications, which could influence hyponatremia risk.

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