

# PREVALENCE OF ASYMPTOMATIC HYONATREMIA IN TYPE 2 DIABETES MELLITUS PATIENTS HAVING UNCONTROLLED BLOOD GLUCOSE LEVELS PRESENTING AT HAYATABAD MEDICAL COMPLEX PESHAWAR

Muhammad Sami<sup>1</sup>, Sana<sup>1</sup>, Khalid Usman<sup>1</sup>

1. Department of Diabetes, Endocrinology and Metabolic Diseases, Hayatabad Medical Complex, MTI, Peshawar.

Correspondence Email: [usmank70@yahoo.com](mailto:usmank70@yahoo.com)

Received- 15<sup>th</sup> Jan 2025; Revisions Received- 25<sup>th</sup> Jan 2025; Accepted- 10<sup>th</sup> Feb 2025

## ABSTRACT

**BACKGROUND:** Type 2 diabetes mellitus is emerging as largest pandemic in the world. Hyponatremia is common in diabetic patients, early detection helps in decreasing morbidities associated with electrolytes imbalance.

**OBJECTIVE:** To determine prevalence of asymptomatic hyponatremia in type 2 diabetes mellitus patients having uncontrolled blood glucose levels. The second objective was to evaluate the correlation between the severity of hyponatremia and the duration of uncontrolled diabetes in type 2 diabetic patients.

**METHODOLOGY:** Study was conducted from June 2024 to December 2024 in department of Endocrinology and Diabetes, Hayatabad Medical complex Peshawar. Total 376 participants, adult diabetic patients of both genders having diabetes for at least last 10 years, clinically stable and with uncontrolled diabetes ( $HbA1c > 7$ ) were included in the study from the out-patient department. Mean and standard deviation were calculated for continuous variables while percentages were obtained for categorical variables. Chi square test was used where necessary keeping p value of  $\leq 0.05$  as statistically significant.

**RESULTS:** Out of total 376 participants, male participants were 58.24 % while female participants were 41.75%. Hyponatremia was found in 59.3 % patients. 46.63% of male while 53.33% of female participants were suffering from hyponatremia. According to severity of the hyponatremia, it was mild in 57.3% cases, moderate in 30.49% cases while profound in 12.1% cases. Hyponatremia was significantly associated with age and HbA1c levels while it was not associated with gender.

**CONCLUSION;** Asymptomatic hyponatremia has high prevalence in the T2DM patients whose blood glucose levels remain uncontrolled. These imbalances can also be ameliorated in advance to minimize the risk of complications and ultimately benefit diabetes management.

**KEYWORDS** Type 2 diabetes mellitus, hyponatremia, uncontrolled diabetes

**HOW TO CITE THIS ARTICLE:** Sami M, Sana , & Usman K. Prevalence of asymptomatic hyponatremia in type 2 diabetes mellitus patients having uncontrolled blood glucose levels presenting at Hayatabad Medical Complex Peshawar. *Northwest J Med Sci.* 2024;4(1):25-29.

## INTRODUCTION

Type 2 diabetes mellitus is a non-communicable serious public health problem. It is the biggest pandemic in the world, and its alarmingly high incidence rate is reason for concern.<sup>1</sup> In 2021, diabetes killed 6.7 million people globally, with 537 million adults living with the condition, according to the International Diabetes Federation. This figure is expected to increase to 643 million by 2030.<sup>2</sup> Diabetes mellitus is known to cause an electrolyte imbalance in the patients and causes a huge economic and health burden to both the individual and the community. Hyponatremia is common in diabetic patients, increasing morbidity and mortality. A variety of neurological, musculoskeletal, and gastrointestinal symptoms might develop into potentially fatal consequences, depending on the pathophysiologic severity of the sodium imbalance.<sup>3</sup> Because mild or moderate hyponatremia symptoms are less severe and can overlap with other clinical presentations, it can be difficult to distinguish clinically from other conditions.<sup>4</sup>

Due to osmotic fluid changes caused by hyperglycemia,

electrolyte imbalance primarily affects diabetics and has two significant effects on the body's electrolyte concentration. Water movement across the cellular membrane may have a dilution effect by either raising or decreasing extracellular electrolyte concentrations, particularly in an insulin-deficient state, if it moves internal electrolytes to the extracellular area.<sup>5</sup> Serum sodium ( $Na^+$ ) levels are diluted by these osmotic processes, which may lead to hyponatremia (a concentration of less than 135 mmol/L).<sup>6</sup> Insulin is necessary for the  $Na^+/K^+$  ATPase to function. This transporter maintains the transmembrane  $K^+$  and  $Na^+$  gradients. This transport protein's activity may be decreased in diabetics who have insulin resistance or inadequate insulin synthesis. Electrical gradients across the membrane control the diffusion of  $K^+$  from cells and the diffusion of  $Na^+$  within cells. Serum sodium levels are affected by variations in the hormone insulin levels.<sup>7</sup>

Additionally, research indicates that type 2 diabetes mellitus (DM) is associated with both hypo- and hypernatremia as well as other electrolyte abnormalities, which are a result of the

coexistence of processes related to hyperglycemia that tend to alter blood sodium in opposite ways.<sup>8</sup> The purpose of this study was to determine the prevalence of hyponatremia in patients with uncontrolled type 2 diabetes who were visiting the department of Endocrinology and Diabetes at our setting, as there was no data on salt disturbances in these patients.

**METHODOLOGY:**

This cross-sectional study was conducted from June 2024 to December 2024 in department of Endocrinology and Diabetes, Hayatabad Medical complex Peshawar Pakistan. Sample size was 376 patients with uncontrolled type 2 diabetes mellitus, calculated through Raosoft sample size calculator taking anticipated proportion of hyponatremia in uncontrolled type 2 diabetes to be 52.67%, confidence interval of 95% and margin of error 5%. Purposive non probability sampling technique was used. Inclusion criteria was adult diabetic patients of both genders having diabetes for at least 10 years, clinically stable and with uncontrolled diabetes (HbA1c > 7) were included in the study from the out-patient department. Patients with microalbuminuria, kidney disease, heart failure, SIADH, Cushing syndrome, liver disease or taking diuretics were not included in the study. Consent of all the included patients were obtained for use of their data for research purpose. Demographic details of the patients including name, age and gender were recorded. Blood was taken from all the patients for determination of plasma concentrations of sodium, glucose and HBA1C levels.

At higher concentrations, glucose causes isotonic or hypertonic hyponatremia. As all patients were diabetic, corrected plasma sodium values for RBS were used. Following formula to calculate this corrected [Na],

- **Corrected sodium** = Measured sodium + [(glucose level - 100) x 0.016]<sup>5</sup>

Uncontrolled diabetes was defined as HBA1c level of more than 7. Plasma sodium concentration <135 mmol/L was defined as hyponatremia and further subcategorized the biochemical severity of hyponatremia as mild= plasma sodium concentration 130-134 mmol/L; moderate= plasma sodium concentration 125-129 mmol/L and profound= plasma sodium concentration <125 mmol/L. Statistical analysis of the data was done through SPSS version 27. Mean and standard deviation were calculated for continuous variables while percentages were obtained for categorical variables. Chi-square test was used where necessary keeping p value of ≤ 0.05 as statistically significant.

Ethical approval of the study with reference number 1950 was obtained from the institutional review and ethic committee of Hayatabad Medical Complex, on 22/05/2024.

**RESULTS**

In the current study, out of total 376 participants, male participants were 219 (58.24%) while female participants were 157 (41.75%), Fig. 1. The mean age of the study participants was 56.90 ± 13.17 years. The mean HBA1C level was 9.83±1.36. Hyponatremia was found in 223 (59.3 %) patients. Out of these 104 (46.63%) were male while 119 (53.33%) were female, Fig.1.

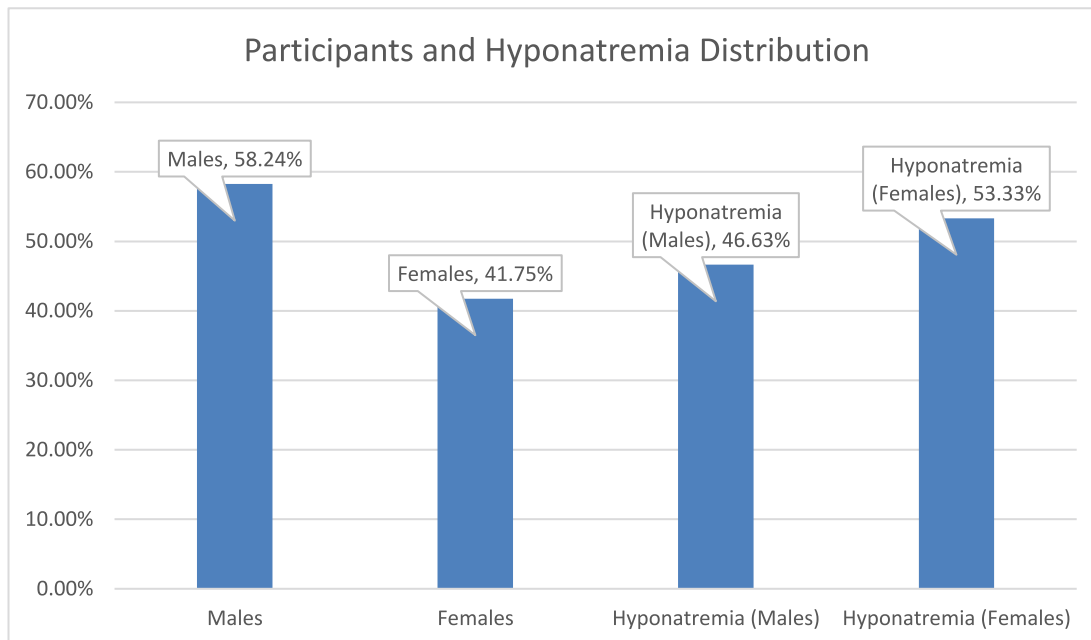
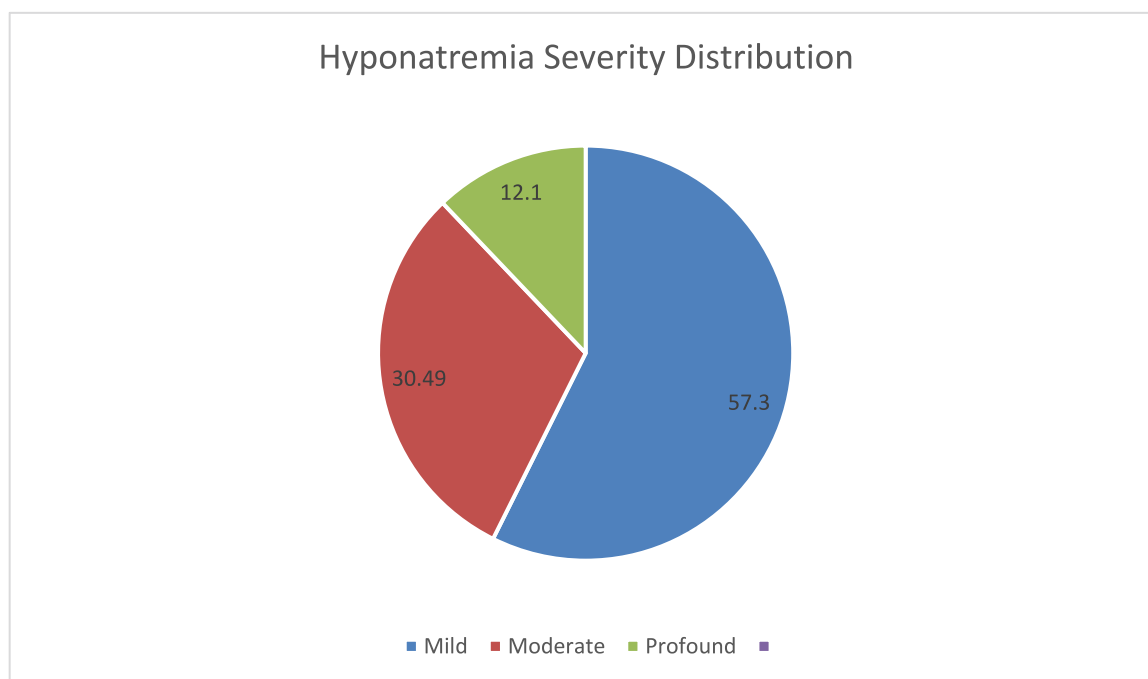


Fig. 1; Participants & hyponatremia distribution

According to severity of the hyponatremia, it was mild hyponatremia (plasma sodium concentration 130-134 mmol/L) in 128 (57.3 %) cases, moderate hyponatremia (plasma sodium concentration 125-129 mmol/L) in 68 (30.49 %) cases while profound hyponatremia (plasma sodium concentration <125 mmol/L) in 27 (12.1 %) cases. Fig.2. The mean serum sodium level was 134.18±7 mmol/L.



**Figure 1 Hyponatremia severity distribution**

Stratification of hyponatremia according to gender yielded p-value of 0.9805, which was statistically not significant. Similarly, when hyponatremia was stratified among different HbA1c levels, the calculated p value was 0.0110, which was statistically significant.

**Table 1. Stratification of Hyponatremia with Gender & Age**

Variables	No of individuals with hyponatremia	No of individuals without hyponatremia	p value
<b>Gender</b>			0.9805
Male	130	89	
Female	93	64	
<b>Age groups</b>			0.0012
30-45 years	45	33	
46-60 years	82	81	
61-75 years	96	39	
<b>HbA1c level</b>			0.0110
≤9	86	43	
>9 to 11	102	94	
>11	35	16	

## DISCUSSION

Results of this study showed a high prevalence of asymptomatic hyponatremia in T2DM patients with uncontrolled blood glucose levels, with considerable variation across HbA1c. These results make it necessary for regular monitoring of electrolytes in such cases to prevent possible hyponatremia complications.

The overall prevalence of hyponatremia was 59.3%, which was consistent with previous studies that show that people with T2DM are prone to having electrolyte imbalance due to osmotic diuresis, the use of diuretics, and possibly altered renal function. From previous studies, reports of the mean of serum sodium was lower in diabetes mellitus compared to healthy controls which was significant endorsing the relevance of our findings.<sup>9</sup>

Besides, age contributed significantly to the variation of hyponatremia ( $p = 0.0012$ ). It was in consonance with previous researches that have made a relationship between aging and disturbed water regulation, lower renal function, and a probably increased likelihood of having comorbidities causing hyponatremia.<sup>6,10,11</sup> These findings stress the remedial vigilance that should be accorded to older T2DM patients, who are most likely to suffer significant adverse effects from disturbances of their electrolyte levels.

Our study identified a statistically significant relationship between HbA1c levels and the prevalence of hyponatremia ( $p = 0.0110$ ). This suggests that hyperglycemia itself plays a more significant role in the development of hyponatremia in T2DM patients compared to age and gender. In similarity to our observations, Rajagopal et al have presented this statistically significant association between HbA1C levels and hyponatremia ( $p=0.0001$ ).<sup>12</sup> However, they included patients with both uncontrolled and controlled diabetes in the study. This may be a representation of interaction of different pathophysiological mechanisms with one another and with the state of blood glucose in sodium imbalance.

Stratifying severity of hyponatremia revealed that in mild cases, it composed the greater proportion of patients (57.3 %) whereas moderate and severe cases, which numbered 30.49% and 12.1%, respectively. The average serum sodium level was  $134.18 \pm 7$  mmol/L. Reshma et.al conducted a study where there was a significant decrease in serum  $\text{Na}^+$  levels in patients with  $\text{RBS} > 300\text{mg/dl}$  ( $131.83 \pm 4.36$  mmol/L) compared to  $\text{RBS} < 300\text{mg/dl}$  group ( $134.15 \pm 4.90$  mmol/L). Our study shows that although severe hyponatremia is less frequent, these mild to moderate cases deserve clinical attention because of their possible effects on neurological function, stability of cardiovascular system, and overall quality of life.<sup>13</sup>

This study reinforces the importance of early identification and management of hyponatremia in T2DM patients, particularly in older individuals and those with higher HbA1c levels. It suggests that serum sodium tests become routine and part of the

management protocol for diabetic patients with uncontrolled blood glucose levels. Physicians also need to be cautious when prescribing medications, including thiazide diuretics that can worsen hyponatremia. This major discovery shows the importance of early recognition and treatment of hyponatremia in patients with T2DM, especially women and older people. Serum sodium testing should be included in the treatment protocol of diabetic patients with poor blood sugar control. Warning to clinicians regarding thiazide diuretics, which contribute to a higher risk of hyponatremia.

The study highlights the significance of early detection and management of hyponatremia in T2DM patients, with a particular focus on those with poor blood glucose control. Routine serum sodium testing should be an integral part of diabetes management protocols. Physicians should exercise caution when prescribing medications such as thiazide diuretics, as they may exacerbate hyponatremia. Additionally, regular monitoring of sodium levels is especially crucial for patients with uncontrolled diabetes to minimize complications and improve overall disease management.

## CONCLUSION

Asymptomatic hyponatremia has high prevalence in the T2DM patients whose blood glucose levels remain uncontrolled, implying a major opportunity for intervention with regard to possible clinical significance. The fact that it has significantly been associated with higher HbA1c and age requirement shapes the focal management strategy. These imbalances can also be preemptively ameliorated to minimize the risk of complications and ultimately benefit diabetes management. Limitations associated with this study are data were collected in a cross-sectional manner, serial fasting & random blood glycemic level and intake of fluids, could not be collected; all these might have influenced the findings.

## Acknowledgement

We would like to thank all the doctors who helped us in data collection.

## Conflict of interest:

The authors declare no conflict of interest related to this publication.

## Financial disclosure statement:

No financial support or external funding received to complete this research work.

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<https://doi.org/10.14341/DM10302>

Key Contributions of the Authors	
Author Names	Author Contributions
Muhammad Sami	A, B, C, D
Sana	B, C, D
Khalid Usman	A, B, D

**Key for Author Contributions:**

- A. Conception or Design
- B. Acquisition, Analysis, or Interpretation of Data
- C. Manuscript writing
- D. Critical Review and approval

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved



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