

## ORIGINAL ARTICLE

# Postoperative Rise in Serum Sodium Level, an Indicator of Diabetes Insipidus after Pituitary Adenoma Surgery

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## ABSTRACT

**Objective:** To study the efficacy of post operative rise in serum sodium level as indicator of diabetes insipidus after pituitary adenoma surgery.

**Materials and Methods:** The study was randomized control trial. It was conducted in Department of Neurosurgery and Biochemistry from March 2016 to December 2017 (22 Months) Punjab Institute of Neurosciences/Lahore General Hospital/Postgraduate Medical Institute/Ameeruddin Medical College. Ethical approval was obtained from hospital Ethics Committee. Total no. of 169 patients were enrolled for transsphenoidal surgery of their pituitary adenoma. Sample size was calculated from the reference study conducted by Schreckinger M et al<sup>10</sup>. Non probability consecutive sampling technique was used to collect the sample size. Data was calculated from all the patients regarding age, gender, duration of transsphenoidal surgery, postoperative evidence of diabetes insipidus by measuring rise in serum sodium level  $< 145\text{mEq}$ . Mean and standard deviation were calculated for demographic variables like age and gender while frequency and percentage were calculated for outcome variables like type of diabetes insipidus and sensitivity and specificity of serum sodium  $> 145\text{mEq}$  test. Chi square test was applied and analysis was done using computer software SPSS version 23. P value less than 0.05 was considered significant.

**Results:** Overall, 100% (n = 169) patients were enrolled in this study, both genders. Gender distribution showed there were 68% (n = 115) males and 32% (n = 54) females. The mean age of the patients was  $40.88 \pm 4.95$  years. Post-operative transient noted in 13.6% (n = 23) patients. Serum sodium level (specific) observed in 92.9% (n = 157) patients. While,  $> 145\text{mEq}$  sensitive was observed in 88.2% (n = 149) patients (Table 1). The main outcome variable of this study was diabetes insipidus permanent, in our study, it was noted in 9.5% (n = 16) patients (Table 2). There was no association between diabetes insipidus permanent and effect modifiers (Table 3).

**Conclusion:** From this study we conclude that level of sodium  $> 145\text{mEq}$  is very sensitive and specific test which can be used to predict the outcome after pituitary adenoma surgery in the form of Diabetes Insipidus.

**Keywords:** Diabetes Insipidus, Pituitary Adenoma, Postoperative Sodium Level Increase, transsphenoidal surgery, hypernatremia, hyponatremia, hypotonic polyuria, polydypsia.

## INTRODUCTION

All over the world incidence of pituitary tumors is arguably the same.<sup>1</sup> Harvey Cushing was the man to pioneer the technique of sublabial and transcranial approach of management in pituitary tumor surgery.<sup>2</sup>

Focus of study is diabetes insipidus which occurs postoperatively in pituitary adenoma surgery along with other hormonal and electrolyte abnormalities.<sup>3</sup>

Diabetes insipidus is a condition in which low level of ADH secreted by the posterior lobe of pituitary gland results in excessive water excretion and thus polyuria and if not managed properly by optimum fluid intake dehydration.<sup>4</sup> One of the major findings in diabetes insipidus is low urine osmolality and high serum osmolality owing to increased serum sodium concentration. There are multiple factors which can predispose a

patient to develop postoperative diabetes insipidus after transsphenoidal surgery like, male sex, young age, macro size of tumor, CSF leak and type of the tumor e.g. Rathke-Cleft cyst, craniopharyngiomas and adrenocorticotrophic hormone secreting pituitary adenoma.<sup>5</sup> Diabetes insipidus occurring postoperatively can be classified as, transient, permanent or triphasic.<sup>6</sup> **Transient type** is the most common, where **prolonged** polyuria occurs in only 2-10%.<sup>7</sup>

**Transient diabetes insipidus** is called so, because it resolves as soon as ADH secreting neurons recover their normal function. **The triphasic type** is very uncommon occurring in just 3.4% patients of transsphenoidal surgery. Usually what happens is, after 5 – 7 days of first phase of diabetes insipidus, it is followed by surge of ADH causing SIADH (syndrome of inappropriate secretion of antidiuretic hormone). This is caused by ADH release from degenerated posterior pituitary tumor or from remaining magnocellular neurons. The duration of second phase is variable, 2 – 14 days. When a patient after transsphenoidal surgery excretes large amount of urine, approximately > 2.5 ml/Kg body weight, diabetes insipidus should be considered as the diagnosis.

But if there is history of excess fluid intake or intravenous administration during preoperative management or if postoperative polyuria is associated with continuous perioperative infusion of fluids, diabetes insipidus is less likely to be the cause of polyuria. **Polyuria associated with high serum sodium level is diabetes insipidus**, if there is no rise in serum sodium level in polyuric patient fluid infusion must be slowed down and sodium level and urine output closely monitored. **Confirmation of diagnosis** can be done by measuring the **high serum sodium level** present in continued hypotonic polyuria.

**Diabetes insipidus** diagnosis is based on clinical as well as biochemical data. Clinical complaints regarding diabetes insipidus are, sudden onset of polydipsia and polyuria, in the time span of 24 to 48 hours postoperatively, patients usually craves for ice cold water.<sup>8</sup> Urinalysis will show hypotonic urine with osmolality < 200 mOsm/kg H<sub>2</sub>O and specific gravity < 1.005. Similarly high serum osmolality and hypernatremia is strongly indicative of diabetes insipidus. But patients with free access to fluid intake usually do not have hypernatremia or high serum osmolality due to intact thirst mechanism.<sup>9</sup> So **water deprivation test** is ideal in such cases to detect hypernatremia and hyperosmolality of serum to confirm the diagnosis of diabetes insipidus.

Our study mainly focuses towards the use of serum sodium level in diagnosis of diabetes insipidus and to determine the sensitivity and specificity of this test in diagnosis. In previous literature multiple studies have tried to determine the predictors of diabetes insipidus in postoperative phase of pituitary tumors surgery. Rationale of this study is to find out the importance of serum sodium level of >145mEq in diagnosing diabetes insipidus.

## **MATERIALS AND METHODS**

This study was conducted at the Departments of Neurosurgery and Biochemistry from March 2016 to December 2017 (22 Months) Punjab Institute of Neurosciences/Lahore General Hospital /Postgraduate Medical Institute/Ameeruddin Medical College. Ethical approval was obtained from hospital Ethics Committee. Total no. of 169 patients were enrolled for transsphenoidal surgery of their pituitary adenoma. Informed consent was taken from the patients prior to surgery to include them in the study. Sample size was calculated from the reference study conducted by Schreckinger M et al.<sup>10</sup> Non probability consecutive sampling technique was used to collect the sample size. Data was calculated from all the patients regarding age, gender, duration of transsphenoidal surgery, postoperative evidence of diabetes insipidus by measuring rise in serum sodium level < 145mEq.

Procedure was performed under general anesthesia, by well experienced neurosurgeon and the person conducting the research collected data from each patient postoperatively. The preoperative workup for patients undergoing transsphenoidal resection of the pituitary includes a thorough history of sinus disease (e.g., hyposmia, epistaxis, nasal polyps, nasal discharge, and sinusitis) and past nasal and sinus surgical treatment. Active or untreated chronic sphenoid sinusitis is a contraindication to performing the transsphenoidal approach to the pituitary. CT scan and MRI were advised preoperatively to diagnose the pituitary adenoma and identify the location of the tumor.

## **Diagnosis**

In order to diagnose diabetes insipidus, postoperative complaints of polyuria and polydipsia, along with **serum ADH level, urine and plasma osmolality** were recorded. Serum ADH level was considered as gold standard for diagnosing postoperative diabetes insipidus. In certain cases **water deprivation test** was also used where diagnosis was in doubt.

**Data Analysis**

All data collected was taken in the form of a Performa. Mean and standard deviation were calculated for demographic variables like age and gender while frequency and percentage were calculated for outcome variables like type of diabetes insipidus and sensitivity and specificity of serum sodium > 145mEq test. Chi square test was applied and analysis was done using computer software SPSS version 23. P value less than 0.05 was considered significant.

**Table 1:** Demographic and Baseline Characteristics of the Patients.

Variable	Frequency	Percentage
Gender	M = 115, F = 54	M = 68%, F = 32%
Post-Operative Transient	N = 23	13.6%
Serum Sodium level specific	N = 157	92.9%
> 145 mEq sensitive	N = 149	88.2%
	Mean ± S.D	
Age (years)	40.88 ± 4.95	

**RESULTS**

Overall, 100% (n = 169) patients were en-rolled in this study, both genders. Gender distribution showed there were 68% (n = 115) males and 32% (n = 54) females. The mean age of the patients was 40.88 ± 4.95 years. Post-operative transient diabetes insipidus noted in 13.6% (n = 23) patients. Serum sodium level (specific) observed in 92.9% (n = 157) patients. While, > 145 mEq sensitive was observed in 88.2% (n = 149) patients (Table 1).

The main outcome variable of this study was diabetes insipidus permanent, in our study, it was noted in 9.5% (n = 16) patients (Table 2). There was no association between diabetes insipidus permanent and effect modifiers (Table 3).

**Table 2:** Distribution of Diabetes Insipidus Permanent.

Diabetes Insipidus Permanent	Frequency	Percentage
Yes	16	9.5
No	153	90.5
Total	169	100.0

**Table 3:** Association of Diabetes Insipidus Permanent with Effect Modifiers.

Variable	Diabetes Insipidus Permanent		Total	Chi-Square P-value
	Yes	No		
Gender	Male	2	52	0.079
	Female	14	101	
Total		16	153	169
Post-Operative Transient	Yes	1	22	0.367
	No	15	131	
Total		16	153	169
Serum Sodium level specific	Yes	15	142	0.889
	No	1	11	
Total		16	153	169
> 145 mEq sensitive	Yes	15	134	0.467
	No	1	19	
Total		16	153	169

**DISCUSSION**

Majority of the patients undergoing transsphenoidal adenomectomy suffer from endocrine and other homeostatic abnormalities including water and electrolyte disturbances, which usually are transient. Many researchers have shown that Diabetes insipidus is much more common complication when compared to hyponatremia caused by syndrome of inappropriate antidiuretic hormone secretion. Studies have shown that diabetes insipidus after pituitary surgery often occurs on first postoperative day and disappears usually within 10 days after surgery.<sup>11</sup> In another study about outcomes of

transsphenoidal surgery, cerebrospinal fluid leak was a more common complication with incidence of 2.7% while diabetes insipidus lasting less than a year post-operatively had incidence of 1.6% and more than year in 0.4% of the cases.<sup>12</sup> Similarly incidence of diabetes insipidus in similar studies about outcomes of transsphenoidal surgery for Cushing syndrome were reported about 15% and other fluid and electrolyte abnormalities occurring in 12.5% of cases while neurological abnormalities had incident of 5.6%.<sup>13,14</sup> While determining the prevalence patterns and predictors of postoperative polyuria, Hensen et al, illustrated that after selective transsphenoidal surgery disturbances in osmoregulation can result in polyuria and polydypsia, which can be detected with the help of perturbations of serum sodium level, thus suggesting high prevalence of this finding in polyuric patients after transsphenoidal surgery for Cushing syndrome.<sup>15</sup>

In a study correlation between sign and symptoms and a specific finding were discussed, and suggested that diabetes insipidus was significantly associated with increased ( $P = 0.001$  and  $0.002$ ) thirst while hyponatremia was correlated with decreased thirst ( $p = 0.003$ ). Hypernatremia and increased serum osmolality had considerable association with diabetes insipidus suggesting its presence and severity ( $p = 0.023$ ). Diabetes insipidus and hyponatremia had no correlation with urine sodium excretion and electrolyte free water clearance though.<sup>16</sup> Neurosurgeries such as pituitary adenoma surgery, subarachnoid hemorrhage surgery and traumatic brain injury surgery can cause diabetes insipidus acutely. As discussed earlier, onset of diabetes is one to three days after insult during neurosurgery and it manifests as polyuria, polydypsia and hypotonic urine.<sup>17</sup> In neurosurgery patients, multiple factors are involved which can result in development of hypernatremia, for instance, diminished consciousness level, cerebral edema, sedation which is achieved for airway management or all of these combined. This is because, presence of these factors impair the sense of thirst or patient's perception regarding fluid ingestion. Therefore daily plasma sodium concentrations and urine output must be monitored on daily basis as patients are vulnerable to develop hypernatremia.<sup>18,19</sup>

## CONCLUSION

From this study we conclude that level of sodium  $>145\text{mEq}$  is very sensitive and specific test which can be used to predict the outcome after pituitary adenoma surgery in the form of Diabetes Insipidus.

## Conflict of Interest

There was no conflict of interest regarding this study.

## Funding Source

No extra funding source was utilized.

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Date of Submission: 15-4-2018

Date of Printing: 30-6-2018

Peer Reviewed by Dr. Babar Butt, Amir Aziz and Dr. Fauzia Sajjad and others.