



Original Research

Predictive Role of Tumor Dimensions and Body Mass Index in The Development of Postoperative Diabetes Insipidus Following Pituitary Adenoma Resection: Analysis of 209 Consecutive Cases

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ABSTRACT

Objective: This study examines the outcomes of tumor size, dimensions, and patients' body mass index (BMI) on the postoperative DI.

Material and Methods: This study was done on 209 patients who met the inclusion criteria. They were counseled and comprehensively informed about the study. The DI was labeled according to the operational definition. The DI was managed as per ward protocol. All the data was recorded. All the surgeries were done by one surgical team, and all the labs were done from one lab, i.e., hospital lab.

Results: Out of 209 patients, 1.9% (n = 4) were between 5 and 30 years of age, and 98.1% (n = 205) were between 31 and 60 years of age. The mean age was 41.45 ± 6.47 years. The distribution of the size of the tumor was 2.69 ± 0.756 cm, and the distribution of BMI was 26.00 ± 1.954 kg/m². Out of 209 patients, 61.2% (n = 128) were male, whereas 38.8% (n=81) were female. The distribution of DI among patients undergoing endoscopic transsphenoidal surgery was 25.4% (n=53).

Conclusion: We found that DI among patients undergoing endoscopic transsphenoidal surgery was 25.4% (n=53). Therefore, post-operative DI is one of the common complications after pituitary surgery.

Keywords: Pituitary adenoma, Transsphenoidal surgery, Diabetes insipidus.

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INTRODUCTION

Pituitary adenomas (PA) are the most commonly occurring benign brain neoplasms. They

constitute around 14% of the primary tumors of the intracranial nervous system, with around 17% prevalence overall in the general population (detected through radiography and autopsy). Most of these tumors are functional (46% - 64%), thus secreting hormones. On the other hand, sometimes these tumors don't secrete any hormones and are non-functional (46%-54%). The most common hormone secreted tends to prolactin (32%-51%), followed by growth hormone (GH) (9%-11%), thyroid-stimulating hormone (TSH)-secreting and gonadotropin-secreting adenomas (<1%).^{1,2,3}

The mode of treatment for these tumors is almost always the minimally invasive, endoscopic transsphenoidal surgery. But there are exceptions for some large macroadenomas, extending to the temporal lobe or the anterior cranial fossa. For such cases, the transcranial approach is the preferred option, but sometimes a combined approach can also be used.^{4,5}

The surgical management of PA is associated with several complications, such as cerebrospinal fluid (CSF) leak, perioperative hemorrhage, bacterial meningitis, orbital injuries, permanent panhypopituitarism, and temporary or permanent diabetes insipidus (DI).^{6,7} First described in the 18th century,⁸ DI is a very rare disorder with various etiologies, and postoperative DI, following neurosurgical intervention, is also one of them. In this case, it tends to be central DI most of the time, which is due to the decreased release of arginine vasopressin (AVP), also called antidiuretic hormone (ADH), by the damaged pituitary gland. It can also be due to unresponsiveness of renal tubular cells to AVP, called nephrogenic DI. The clinical manifestations of DI can include polydipsia and polyuria, leading to a state of dehydration. Ultimately, it can also result in a hyponatremic state if the patient is deprived of water.⁹ The diagnostic tests include the water deprivation test, urine, and blood tests. Temporary management includes IV fluid therapy, and long-term treatment includes DDAVP (1-

deamino-8-arginine vasopressin).¹⁰

The literature gives a wide range of incidence of DI postoperatively among patients with PA, spanning from 0.3% to 45%, which reflects a heterogeneity in diagnostic criteria, characteristics of the tumor, or surgical expertise. Given the significant impact on patient recovery and healthcare resources, determining the local frequency and associated factors of DI is vital for risk stratification and management. Ajlan et al, report in their study that the frequency of DI postoperatively among patients with pituitary adenomas is around 26%.¹¹

This study examines the association of tumor size, dimensions, and patients' body mass index (BMI) with the postoperative DI. It can prove to be fatal for the patient. Because of a high volume of cases of PA in our department, there was a need to conduct this study to help identify the association of tumor dimensions and patient BMI with this postoperative complication, thus helping us predetermine the risk and accordingly take measures to minimize the risk of morbidity in the patients. The study aims to examine the frequency of DI in patients after endoscopic transsphenoidal surgery of PA.

MATERIAL AND METHODS

Pituitary Adenoma is a benign growth/tumor in the anterior pituitary, which can be either a macroadenoma (diameter ≥ 1 cm) or a microadenoma (diameter <1cm). The diagnosis is made based on history, examination, and investigations (can include plain MRI- Brain, or with IV contrast, CT FESS protocol, and hormonal profile).

Study Design & Setting

It is a quantitative, retrospective, and descriptive study conducted at the Department of Neurosurgery, Unit 2, Punjab Institute of Neurosciences, Lahore. It was carried out over a

period of three years between 01.03.2022 and 28.02.2025. The Institutional Review Board number for this study was (2277/IRB/PINS/Approval/2025).

Sample Size

This study constituted a sample size of a total of 209 cases. This sample was calculated using a 90% confidence interval. The margin of error for the study was 5%. The expected rate of DI among cases was 26%, which was determined through the study conducted by Ajlan et al.⁸

Inclusion Criteria

Patients of either gender, with an age ranging between 13 and 60 years, and presenting with a pituitary adenoma as per the operational definition. Patients who gave written informed consent for participation in this study.

Exclusion Criteria

Patients who will have intra- or postoperative mortality within 1 week after the surgery. Non-pituitary tumors (craniopharyngioma, meningioma, chordoma) as per clinical examination. Adenomas with extension to the cavernous sinus and having an hourglass appearance. Patients who refuse to consent to participate in the study.

Data Collection Procedure

209 patients who met the defined inclusion criteria were counseled and informed comprehensively about the study details. The participants provided their written informed consent to participate. A detailed history was obtained from all participants. Patients underwent endoscopic transsphenoidal surgery for PA. Patients were discharged once the discharge criteria were met. They were monitored for polyuria or abnormal thirst during the first week of surgery and were investigated to see if any

symptoms appeared. DI was labeled according to the operational definition. It was managed as per ward protocol. The study data were collected and written down in the proformas, which were attached to the demographic characteristics of the study participants. All the surgeries were performed by one surgical team, and all the labs were done from one lab, i.e., hospital lab, to eliminate bias, and confounding variables were controlled by exclusion. Regular follow-up was conducted by medical oncologists and endocrinologists in multidisciplinary board meetings. Nonprobability and consecutive sampling techniques were used in this study.

Data Analysis Procedure

The study data were analyzed by the software Statistical Package for Social Sciences (SPSS) version 27. The numeric variables, i.e., tumor size, BMI, and age, were written as mean \pm SD. The categorical variables, i.e., gender and diabetes insipidus, were presented as frequency and percentage. Data were stratified for age, tumor size, BMI, and gender. Post-stratification Chi-square test was used, considering a *p*-value of ≤ 0.05 to be statistically significant. We defined Diabetes insipidus as follows: Postoperative patients (≥ 1 week) who develop complaints of increased urinary frequency, thirst, and urine output are increased (> 300 mL/h for 3 consecutive hours) compared to normal. There is hypernatremia (> 145 mmol/L), with a decreased urine specific gravity (< 1.005).

RESULTS

Demographics

A total of 209 patients meeting the inclusion and exclusion criteria were selected to determine the frequency of DI among patients undergoing endoscopic transsphenoidal surgery for PA.

The distribution of age among patients revealed that out of the total 209 participants,

1.9% (n=4) were younger, falling between 5 and 30 years of age, and 98.1% (n=205) were older, falling between 31 and 60 years of age. The mean age was 41.45 ± 6.47 years. Gender distribution showed that out of 209 patients, 61.2% (n=128) were male, whereas 38.8% (n=81) were female.

Distribution of Tumor Size and Endoscopic Transsphenoidal Surgery

The distribution of the size of the tumor was 26.89 ± 7.55 mm, and the distribution of BMI was calculated as 26.00 ± 1.954 kg/m² (**Table 1**).

The distribution of DI among patients undergoing endoscopic transsphenoidal surgery was 25.4% (n=53).

The chi-square tests revealed that postoperative diabetes insipidus incidence had no significant correlation with either tumor size (**Table 2**) or BMI (**Table 3**).

DISCUSSION

Pituitary adenoma (PA) comprises around 10% of the primary intracranial tumors. This makes PA the most commonly encountered sellar pathologies. In the 1960s, the majority of adenomas were treated through the nasal route. Over the past two decades, there has been a major shift from the microscopic to endoscopic approach for performing TSS, given its comparatively better visualization and thus, fewer chances of complications.¹²

There have been various frequencies of reported potential post-operative complications

Table 1: Distribution of tumor size, BMI (N=209).

Variables	Mean ± S.D
Tumor size (mm)	26.89±7.55 mm
BMI (kg/m ²)	26.00±1.954 kg/m ²

Table 2: Diabetes insipidus with respect to tumor size using chi-square test (N= 209).

			Diabetes insipidus		Total	p-value
			Yes	No		
Tumor size group	10-20mm	Count	22	68	90	0.792
		% of Total	10.5%	32.5%	43.1%	
	>20mm	Count	31	88	119	
		% of Total	14.8%	42.1%	56.9%	
Total	Count	53	156	209		
	% of Total	25.4%	74.6%	100.0%		

Table 3: Diabetes insipidus with respect to BMI using chi-square test (N= 209).

			Diabetes insipidus		Total	p-value
			Yes	No		
BMI group	17-25kg/m ²	Count	13	48	61	0.388
		% of Total	6.2%	23.0%	29.2%	
	>25kg/m ²	Count	40	108	148	
		% of Total	19.1%	51.7%	70.8%	
Total	Count	53	156	209		
	% of Total	25.4%	74.6%	100.0%		

of endoscopic TSS. Post-operative diabetes insipidus (DI) incidence rate reportedly varies widely, ranging from 0.3 to 45%. It may be secondary to inconsistent definition, variation of the follow-up interval, and the diverse nature of sellar pathologies.¹³

In our study, out of 209 patients, 1.9% (n=4) were younger, falling between 5 and 30 years of age, and 98.1% (n=205) were older, falling between 31 and 60 years of age. The mean age was 41.45 ± 6.47 years. The distribution of the size of the tumor was 26.89 ± 7.55 mm, and the distribution of BMI was 26.00 ± 1.954 kg/m². Out of 209 patients, 61.2% (n = 128) were male, whereas 38.8% (n = 81) were female. The distribution of DI among patients undergoing endoscopic transsphenoidal surgery was 25.4% (n = 53).

Giant PAs tend to increase the occurrence of postoperative DI. In the study comprising 50 cases of giant PA, Gondim et al,¹⁴ reported that 10% of subjects got permanent DI postoperatively. This study hypothesized the giant size of tumor (all > 4 cm in largest diameter) as being a contributor to this complication because of the proposed damage during dissection above the sella, which can lead to impairment of the hypothalamus.

35% of 1571 subjects studied by Hensen et al, developed DI in a transient form, and they had resection by microscope in all subjects.¹⁵ Their diagnostic criteria comprised a daily urine of more than 2,500 mL with specific gravity > 1.005 g/L. On the other side, Sigounas et al,¹⁶ reported less frequency of transient (13.6%) as well as permanent (2.7%) post-operative DI among patients with endoscopically resected tumors. They considered congenital and non-neoplastic tumors in their analysis. Their diagnostic criteria included urine output more than 300 mL/h for three consecutive hours with a urine-specific gravity < 1.004. They defined transient DI as the DI lasting for less than six months. One of the review articles discussing the incidence of DI post-TSS, approached through various techniques for numerous sellar pathologies, reported the incidence for transient DI to be 29% and permanent was 1.8%, whereas sublabial had 25% and 2% documented for trans-septal approaches, on the other side 5% for microscopic nasal approach, and 5% and 1.5% for an endoscopic route.¹⁷

Eleven studies pooled analysis juxtapose the microscopic with minimally invasive endoscopic route of surgery for PA and reported overall occurrence of 15% post-operative DI among the endoscopic route cohort and 28% among the cohort of microscopic surgery ($p = 0.003$).¹⁸ A dissimilar meta-analysis, which compared the endoscopic routes & sublabial ones, determined an incidence of enduring post-procedural DI of 2% after endoscopy and 3% after sublabial

microsurgical intervention ($p = 0.1$).¹⁹ Additionally, another contemporary meta review, comprising twenty-three articles, compared the endoscopic to microscopic extirpation of PAs among 2,272 patients, and showed a 22% decline in the DI incidence rate in the endoscopy group²⁰. But this study was not statistically significant.

In their study, Ajlan et.al reported long-term occurrence of post-operative DI to be 10.1%. This remarkable, unprecedented value could potentially be explained by their rigorous criteria, i.e, substantial size of tumor (77% were macro adenomas) & hormonal variety (39% were endocrinologically functional). It also lacked the comparison of the postoperative DI incidence rate between the route cohorts. Analysis by Patil et al,²¹ regionally evaluated outcomes of Cushing's disease treated by microscopic TSS between 1993 and 2002, pen down the risk of postoperative DI to be 15%. This reported value most likely corresponds to the early postoperative DI; the data were derived from the indoor admission record without any follow-up. Furthermore, a prior analysis that compared the endoscopic surgical approach to the microscopic approach showed no prominent variation between the incidence rates of DI between the two groups.²² This is likely explained by a small sample size.

Intraoperative or postoperative CSF leak has been identified as a prominent risk factor for the postoperative DI occurrence. Ajlan et.al reported that patients with per op leak, i.e, 19% ($p = 0.01$), happened to develop long-term DI, while 66% of those with postoperative leak developed DI in the early phase ($p = 0.005$). Intraoperative CSF leaks during endoscopic surgery tend to escalate the risk of post-operative DI from 21% to 37%.²³ Even with microscopic surgery, intraoperative CSF leak increases the risk from 11% to 33%.²⁴ Per or post op CSF leak not only manifests the potential suprasellar extension but also indicates enterprising resection of the tumor by the operating neurosurgeon that poses a greater risk

of injury to the hypothalamo-pituitary axis.

In a clinical trial evaluating hospital stay duration following transsphenoidal PA surgery, Thomas et al,²⁵ proposed a "short-stay protocol", Standardized by sending 92% participants home on postoperative day 1 (mean stay of 1.16 days). They were educated regarding the presentation of DI, and liaison was developed telephonically until the fourth day. This study showed that the development of early DI was independent of the length of stay (LOS). DI can be easily detected clinically. Additionally, it can be managed easily on an outpatient basis, without a high risk of morbidity and mortality. Hence, in the absence of fluid intake and output imbalance and serum electrolyte abnormalities, the mere possibility of developing postoperative DI does not require a longer LOS. On the contrary, the presence of certain risk factors, like young patients, large tumors, intraoperative CSF leak, and immediate postoperative hypernatremia, warrants close monitoring.¹³ Endoscopic skill maturity reflects advancement along the endoscopic endonasal transsphenoidal surgery learning curve, measurable by operative time, intraoperative cerebrospinal fluid leak, need for reoperation, extent of resection, and endocrine or visual outcomes.

With greater proficiency, handling around the pituitary stalk and posterior lobe becomes more delicate, traction is minimized, and hemostasis with layered sellar closure is a more consistent mechanism likely reducing stalk edema or ischemia and postoperative diabetes insipidus.

RECOMMENDATIONS

Incorporation of Advanced Predictors: Future studies should evaluate additional predictors such as surgical factors (extent of resection, intraoperative CSF leak, sellar floor reconstruction methods), tumor characteristics (hormone-secreting vs. non-functional adenomas), and perioperative sodium/osmolality fluctuations to

build a more comprehensive risk stratification model for DI after pituitary surgery.

LIMITATIONS

One of the limitations was a short-term Observation Window, which may underestimate the incidence of late-onset DI or misclassify transient DI as resolved, without clarity.

CONCLUSION

In our study, we determined the frequency of diabetes insipidus (DI) among patients undergoing endoscopic transsphenoidal surgery for pituitary adenoma. It was found to be around 25.4% (n=53). Therefore, we concluded that post-operative DI is a common complication after pituitary surgery.

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Additional Information

Disclosures: Authors declare no conflict of interest.

Institutional Ethical Review Board Approval: The study complies with the ethical review board requirements.

Human subject: Consent was obtained from all patients/participants in this study.

Conflict of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationship at present or within the previous three years with any organization that might have an interest in the submitted work.

Other Relationships: All authors have declared that no other relationships or activities could have appeared to have influenced the submitted work.

Data sharing statement: For data sharing, interested researchers can contact the corresponding authors.

AUTHOR'S CONTRIBUTION

Sr.	Author Name	Author contribution
1.	Waseem Shamas Din	Paper writing, study design, and methodology.
2.	Usman Ahmad	Literature review, data analysis, and discussion.
3.	Hamza Noman & Aysha Ghayyur	Data analysis.
4.	Mehwish Manzoor	Interpretation of results.
5.	Tehreem Asif, & Anosh John	Data collection.
6.	Laiba Fatima	Data analysis and referencing.
7.	Syed Shahzad Hussain Shah	Quality insurer.