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RESEARCH PAPER

Predictors of Postoperative Diabetes Insipidus Following Surgery of Sellar-Suprasellar Tumor

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Abstract

Background: Higher postoperative morbidity and longer hospital stay are linked to diabetes insipidus (DI) after surgery of sellar or suprasellar tumors.

Objective: To find out the predictors of postoperative DI following sellar or suprasellar surgery.

Methods: This case-control study was conducted at the National Institute of Neurosciences and Hospital, Dhaka, from January 2023 to June 2023. Patients with sellar or suprasellar tumors admitted to the neurosurgery department for surgery were included by non-probability consecutive sampling (n=109, age 39.4±13.7 years, 44.9% female). All patients were treated surgically by standard protocol. A standard institutional inpatient monitoring system was used in all postoperative patients regardless of symptoms, including hourly intake and output measurements. Participants were followed up regularly during their hospital stay and then after 6 weeks of surgery up to 6 months. Specific criteria were used to confirm the diagnosis of DI for each patient. All clinical and laboratory data were recorded in a data sheet. Finally patients developing DI were grouped as case and rest of them grouped as control. All clinical and laboratory parameters were compared between two groups.

Result: Transient DI (resolved within 6 weeks of surgery) was present in 53 (49%) and prolonged DI (persisted >6 weeks of surgery) in 22 (20%) participants. Transient DI were more frequent in participants with 1st postoperative serum sodium level >145 mmol/L (p<0.001). Participants with younger age (p=0.044), non-pituitary sellar tumor (p=0.044), preoperative hypothyroidism (p=0.048), gross total removal of tumor (p=0.027) and 1st postoperative serum sodium level >145 mmol/L (p<0.001) had higher frequency of prolonged DI. However, in logistic regression, preoperative hypothyroidism (OR 3.4; 95% CI 1.0-11.6; p=0.048) and 1st post-operative serum sodium >145 mmol/l (OR 11.4; 95% CI 2.8-46.4; p<0.001) showed a significant association with prolonged DI when adjusted for age, tumor type, route and extent of resection.

Conclusion: First post-operative serum sodium >145 mmol/L is a significant predictor of transient DI; whereas first post-operative serum sodium >145 mmol/L and preoperative hypothyroidism are found to be significant predictor of prolonged DI.

Keywords: Diabetes insipidus, Sellar tumor, Suprasellar tumor

Introduction

Postoperative diabetes insipidus (DI) may occur after sellar or suprasellar mass resection due to injury or traction to the pituitary stalk. The reported incidence varies from center to center and commonly ranges from 9-22%, but may occur even in 54% of cases.[1-10] Postoperative DI is often the cause of longer hospital stays, imposes significant morbidity, and is the commonest leading cause of hospital readmission of these patients.[6] The correct and efficient identification of patients with DI following transsphenoidal surgery is important to avoid adverse consequences. However, it is not always easy to diagnose DI, particularly in hospitalized postsurgical patients.[1,7] A puzzling diagnostic assessment may result from the effects of anesthesia, postoperative problems, medicines, nasal packing, and perioperative intravenous fluid administration.[1,7] Early detection of DI is meaningful to patient care and outcomes following such surgery. While the management of DI which complicates

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surgery for pituitary and suprasellar tumors is a commonly encountered topic, it remains a challenging area for clinicians and requires high standards of medical knowledge with superior clinical experience and skills.

An understanding of the postoperative antidiuretic hormone (ADH) pathophysiology and differential diagnoses of polyuria helps to clinically diagnose and test for DI. Following the diagnosis, close monitoring is required to evaluate treatment response and to determine whether the DI is transient, prolonged, or permanent. The majority of postoperative DI is transient, requiring treatment of one week to three months.[7] Permanent DI is much less common, with a reported incidence of only 2-7%.[7] DI is often a part of the triphasic response, which is a postsurgical phenomenon that presents with a short period of DI, followed by the syndrome of inappropriate ADH secretion 5 to 7 days later, resulting in hyponatremia. Eventually, a proportion of these patients go on to develop prolonged or permanent DI. Although the full triphasic response is less common than permanent DI, with an incidence of 1.1%, managing these patients can be complicated and necessitates close observation.[1]

Studies that have examined preoperative and perioperative parameters' correlations with DI retrospectively have identified people who are more likely to experience postoperative DI. Closer postoperative surveillance of the high-risk group may result in prompt diagnosis and reduced postsurgical morbidity. Higher tumor volume, histopathology of Rathke's cleft cyst (RCC) or craniopharyngioma, and higher postoperative serum sodium have been reported to be associated with postoperative DI.[6] However, the findings of different studies were not similar. Kadir et al. observed that functioning pituitary adenomas were much less likely to be associated with DI than nonfunctioning pituitary adenomas.[1] A large, retrospective study showed an intraoperative cerebrospinal fluid (CSF) leak to be strongly associated with DI, in addition to histopathology showing RCC or craniopharyngioma.[4] The study also observed corticotroph adenomas associated with Cushing disease to have a higher association with transient but not permanent DI. It's interesting to note that repeated procedures did not appear to increase the incidence of DI, and microadenomas were more likely than macroadenomas to develop transient DI.[4]

The incidence and risk factors of postoperative DI vary from center to center and may not be generalizable. Risk factors for DI following pituitary surgery have been explored in several studies abroad. However, the surgical setting in our institution and patient characteristics may not be similar to the setting of those studies. So, it is rational to explore this important post-operative complication in our setting. Hence, the purpose of this study was to find out our institution's experience with patients with sellar and suprasellar tumors following surgery to identify pre and immediate post-operative factors that might be associated with the development of postoperative DI.

Materials and Methods

This case-control study was conducted at the National Institute of Neurosciences (NINS) and Hospital, Dhaka, from February 2023 to August 2023. The study included 109 participants aged >18 years, of either sexes with sellar or suprasellar mass; by non-probability consecutive sampling from patients who were admitted to the Neurosurgery department of NINS for surgery. Patients with preoperative DI and those unwilling to take part in the study were excluded.

All patients were clinically assessed thoroughly. Laboratory and imaging data were collected from medical records and were recorded in a case record form. All patients were treated surgically by standard protocol. Participants were followed up regularly during their hospital stay and then after 6 weeks of surgery up to 6 months. During the post-operative period, patients were monitored for the development of DI. A standard institutional inpatient monitoring system was used in all postoperative patients regardless of symptoms, including hourly intake and output measurements for 72 hours. Urine osmolality, urine specific gravity, and serum sodium were tested every 6 hours for 48 hours after surgery. The monitoring was extended if there were abnormal findings. Specific criteria were used to confirm the diagnosis of DI for each patient. These are documentation of increased thirst and subjective polydipsia or polyuria or objective intake and output record showing >250 cc of urine output per hour for at least 2 hours along with a urine osmolality <200 mOsm/kg and/or urine specific gravity <1.005 or a serum sodium >145 mmol/L. Once DI was confirmed, treatment was started according to standard treatment protocol. Transient DI was defined as DI that resolved within 6 weeks of surgery, whereas prolonged DI was labeled when DI persisted at 6

weeks after surgery. Patients developing DI were grouped as case and rest of them grouped as control. All clinical and laboratory parameters were compared between two groups.

Analyses were performed with SPSS software, version 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data that were normally distributed were summarized in terms of the mean and standard deviation. Skewed data were presented in terms of the median and interquartile range. Categorical or discrete data were summarized in terms of frequency counts and percentages. For comparison between groups, chi-squared test or Fisher's exact test were used for categorical variables, and Student's unpaired t-test or Mann-Whitney U test were used for continuous outcomes. A logistic regression model was used to determine the predictors of post-operative DI. A two-sided p-value of <0.05 was considered to indicate statistical significance.

Before the commencement, the study protocol was approved by the Institutional Review Board, NINS, and informed written consent was obtained from the participants.

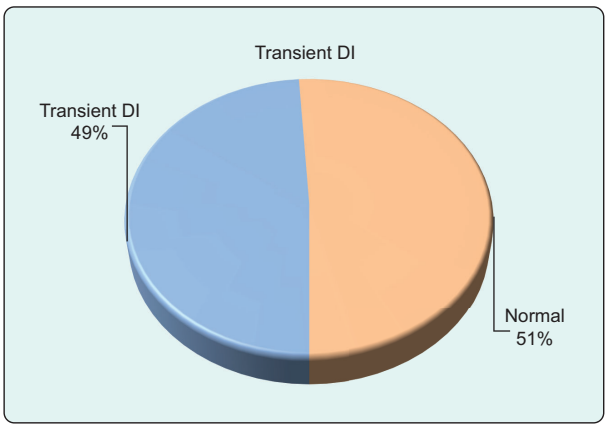
Results

The study included 109 participants who underwent sellar and suprasellar surgery. Mean (±SD) age of the subject was 39.4 (±13.7) year. The majority of the participants (93%) had tumor mass ≥10 mm. The lesion type was mixed with 68% pituitary mass and the rest non-pituitary mass (table I). Transient DI was present in 53 (49%) participants and prolonged DI in 22 (20%) participants (Figure-1).

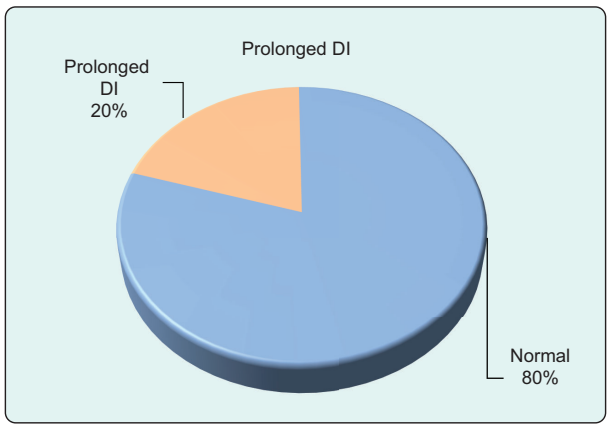
Table I: Characteristics of the study participants (N=109)

Variables		Frequency (%)
Age (years; mean±SD)		39.4±13.7
Sex Female		49 (44.9)
Male		60 (55.1)
Duration of symptoms [months; median (IQR)]		6 (2-24)
Presence of visual defect		44 (40.4)
Lesion type	Pituitary	74 (67.9)
	Non-pituitary	35 (32.1)
Lesion size	<10 mm	8 (7.3)
	≥10 mm	101 (92.7)
Maximum diameter of tumor (cm; mean±SD)		3.2 (2.4-4.1)
Extension beyond sella		98 (89.9)
Preoperative hypoadrenal		74 (67.9)
Preoperative hypothyroid		31 (28.4)
Route of surgery	Transcranial	28 (25.7)
	Transsphenoidal	81 (74.3)
Extent of resection	Partial	67 (61.5)
	Total	42 (38.5)
Recurrent surgery		3 (2.8)
1st Post-op sodium >145 mmol/L		25 (22.9)
Post-op CSF rhinorrhea		21 (19.3)

Within parentheses, percentages over column total, if not mentioned otherwise
DI: Diabetes insipidus CSF: cerebrospinal fluid



(a)



(b)

Figure 1: Frequency of DI following surgery for sellar/suprasellar mass; (a) transient DI, (b) prolonged DI
DI: diabetes insipidus

There was no difference with respect to age, sex, duration of symptoms, presence of visual loss, lesion type, lesion size, lesion extension, preoperative hypoadrenalism and hypothyroidism, route and extent of surgery, and post-operative CSF rhinorrhea between patients with or without transient DI. However, a significantly higher number of patients with 1st post-operative sodium >145 mmol/L developed transient DI (p<0.001) (Table-II).

Table II: Comparison of characteristics of participants with or without transient DI (N=109)

Variables		Transient DI n=53	Without transient DI n=56	p
Age (years; mean±SD)		36.9±14.0	41.7±13.1	0.065†
Sex	Female	21 (42.9)	28 (57.1)	0.316*
	Male	32 (53.3)	28 (46.7)	
Duration of symptoms [months; median (IQR)]		7 (2-21)	6 (1-24)	0.310‡
Presence of visual loss		26 (59.1)	18 (40.9)	0.072*
Lesion type	Pituitary	36 (48.6)	38 (51.3)	0.994*
	Non-pituitary	18 (51.4)	17 (48.6)	
Lesion size	Microadenoma	5 (37.5)	3 (62.5)	0.415§
	Macroadenoma	53 (52.5)	48 (47.5)	
Maximum diameter of tumor (cm; mean±SD)		3.1±1.4	3.2±1.3	0.765†
Extension beyond sella		49 (50.0)	49 (50.0)	0.391*
Preoperative hypoadrenal		35 (47.3)	39 (52.7)	0.687*
Preoperative hypothyroid		17 (54.8)	14 (45.2)	0.413*
Route of surgery	Transcranial	13 (46.4)	15 (53.6)	0.787*
	Transsphenoidal	40 (49.4)	41 (50.6)	
Extent of resection	:Partial	29 (43.3)	38 (56.7)	0.174*
	Total	24 (57.1)	18 (42.9)	
1st post-op sodium >145 mmol/L		38 (76.0)	12 (24.0)	**<0.001***
Post-op CSF rhinorrhea		10 (47.6)	11 (52.4)	0.799*

† by unpaired t-test; *by Chi-squared test; §by Fisher's exact test; ‡by Mann-Whitney U test
Within parentheses, percentages over row total, if not mentioned otherwise
DI: Diabetes insipidus CSF: cerebrospinal fluid

The patients with younger age (p=0.044), non-pituitary sellar tumor (p=0.044), preoperative hypothyroidism (p=0.048), gross total removal of tumor (p=0.027), and 1st postoperative serum sodium level >145 mmol/L (p<0.001) had a higher frequency of prolonged DI (Table-III). However, in logistic regression, preoperative hypothyroidism (OR 3.4; 95% CI 1.0-11.6; p=0.048) and 1st post-operative serum sodium >145 mmol/l (OR 11.4; 95% CI 2.8-46.4; p=0.001) showed a significant predictivity of developing prolonged DI when adjusted for age, tumor type, route and extent of resection (Table-IV).

Table III: Comparison of characteristics of participants with or without prolonged DI (N=109)

Variables		Prolonged DI n=22	Without prolonged DI n=87	p
Age (years; mean±SD)		34.1±13.7	40.7±13.4	**0.044**†
Sex	Female	7 (14.3)	42 (85.7)	0.166*
	Male	15 (25.0)	45 (75.0)	
Duration of symptoms [months; median (IQR)]		6 (2-12)	6 (2-24)	0.782‡
Presence of visual loss		11 (25.0)	33 (75.0)	0.303*
Lesion type	Pituitary	11 (14.9)	63 (85.1)	**0.044***
	Non-pituitary	11 (31.4)	24 (68.6)	
Lesion size	Microadenoma	2 (25.0)	6 (75.0)	0.662*
	Macroadenoma	20 (19.8)	81 (80.2)	
Maximum diameter of tumor (cm; mean±SD)		3.4±1.5	3.1±1.3	0.473†
Extension beyond sella		21 (21.4)	77 (78.6)	0.457*
Preoperative hypoadrenal		16 (21.6)	58 (78.4)	0.586*
Preoperative hypothyroid		10 (32.3)	21 (67.7)	**0.048***
Route of surgery	Transcranial	9 (32.1)	19 (67.9)	0.067*
	Transsphenoidal	13 (16.0)	68 (84.0)	
Extent of resection	Partial	9 (13.4)	58 (86.6)	**0.027***
	Total	13 (31.0)	29 (69.0)	
1st post-op sodium >145 mmol/L		19 (38.0)	31 (62.0)	**<0.001***
Post-op CSF rhinorrhea		4 (19.0)	17 (81.0)	0.266§

† by unpaired t-test; *by Chi-squared test; ‡by Mann-Whitney U test; §by Fisher's exact test
Within parentheses, percentages over row total, if not mentioned otherwise
DI: Diabetes insipidus, CSF: cerebrospinal fluid

Table IV: Logistic regression for prediction of prolonged DI after surgery (N=109)

Variables	OR (95% CI)	p
Age (per year increase)	1.0 (0.9-1.0)	0.352
Non-pituitary mass	4.6 (0.7-28.7)	0.106
Preoperative hypothyroid	3.4 (1.0-11.6)	0.048
Transcranial surgery	0.6 (0.1-4.1)	0.567
Gross total resection	1.9 (0.6-6.1)	0.251
Recurrent surgery	12.9 (0.3-500.0)	0.169
1st post-op sodium >145	11.4 (2.8-46.4)	0.001

R^2=0.409; Hosmer-Lemeshow goodness of fit S«2=11.8; p=0.162
DI: Diabetes insipidus

Discussion

Post-operative DI is one of the important and often inevitable complications of transsphenoidal or transcranial resection of a sellar or suprasellar mass. If it is not properly managed, there could be a serious electrolyte and fluid imbalance that causes unnecessary morbidity and possibly death. The present study observed that one in every two patients developed transient DI following surgery for sellar and suprasellar mass while one in five experienced prolonged DI. Patients with younger age, non-pituitary sellar tumor, hypothyroidism before surgery, gross total removal of tumor, and 1st post-operative sodium >145 mmol/L had a higher frequency of prolonged DI following surgery for sellar/suprasellar tumor.

The study followed the postsurgical patients up to 6 weeks after surgery. Hence, to find out the number of cases of permanent DI was beyond its capacity. However, the incidence of transient DI reported by the current study is comparable to those observed in some studies, while higher than those reported in some other studies.[11-14] This variation in the incidence of postoperative DI may reflect inconsistent case definitions, varying intervals of follow-up, and diverse sellar pathologies. The experience of the surgeons of a particular center may also be related to it. Transient DI typically occurs within 24-48 hours after surgery and may last for the next 2-3 days. It usually does not impose serious management difficulties as long as the patient is conscious, able to feel thirst, and allowed to drink plain water according to thirst. Serious electrolyte imbalance ensues if the patient becomes drowsy or unable to feel/express thirst.

Usually, postoperative DI is termed as transient or permanent. We adopted the terminology proposed by de Vries et al., where the authors proposed five grades of postoperative DI and defined prolonged DI as DI that requires treatment for a minimum of 2 weeks, but fewer than 6 months.[15] The present study had a follow-up duration of 6 weeks. Therefore, few instances classified as prolonged DI in this study might actually be permanent or chronic DI. Nevertheless, only a fraction of those having transient DI went on to develop prolonged DI in the present study.

The demographic and clinical characteristics of patients with or without transient DI were similar in the current study, except for elevated first post-operative sodium, which was related to both transient and prolonged DI. However, when demographic and clinical characteristics of patients with or without prolonged DI were compared, the difference was observed concerning age, tumor type, the extent of tumor resection, preoperative hypothyroidism, and 1st post-operative sodium >145 mmol/L. These differences were appreciated in different previous studies, although not universally.[11,13,16,17] In addition, some studies observed male gender, larger tumor size, intrasellar expansion, visual field defect, intraoperative CSF leak, and Cushing's disease to be significant predictors of post-operative DI.[4] Among all the predictors, preoperative endocrine dysfunction in the form of hypothyroidism and first post-operative sodium >145 were found as independent predictors of DI in our study.

The strength of the study was its prospective nature and inclusion of all types of sellar/suprasellar mass. The research team included both neurosurgeons and endocrinologists, ensuring a collaborative approach. However, the follow-up duration of the patients could be extended to know the chronic nature of DI.

The study had some limitation like, it was a single center study with shorter follow up period.

Conclusions

First post-operative serum sodium >145 mmol/L is a significant predictor of transient DI; whereas first post-operative serum sodium >145 mmol/L and preoperative hypothyroidism are found to be significant predictor of prolonged DI.

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Informed consent

Informed written consent was taken from the participant before enrollment.

Conflict of Interest: There was no conflicts of interest.
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Ethical Clearence: Ethical clearance was obtained from the Institutional Review Board (IRB) of NINS.
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