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Original Article

Early Postoperative Complications of Endoscopic Endonasal Transsphenoidal Surgery for Resection of Pituitary Adenoma

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ABSTRACT

Objectives: To determine early postoperative complications of endoscopic endonasal transsphenoidal surgery for resection of pituitary adenoma.

Materials and Methods: This Descriptive Case Series was carried out at the Department of Neurosurgery, Lady Reading Hospital, MTI, Peshawar. 124 patients of either gender between the age of 16 – 60 were already diagnosed with cases of pituitary adenoma. Patients included in this study were surgically treated by Endoscopic endonasal transsphenoidal surgery. Patients were followed up for seven days after surgery and assessed for CSF leak, the incidence of diabetes insipidus epistaxis, and meningitis. Stratification was done for age and gender and p-value < 0.05 (chi-square).

Results: CSF leak was observed in 2.4% (n = 3) of patients, diabetes insipidus was found in 11.3% (n = 14), Epistaxis in 1.6% (n = 2), and meningitis in 1.6% (n = 2) patients. No statistically substantial difference for both postoperative complications was observed based on gender and age-based stratification.

Conclusion: Diabetes insipidus was a common early postoperative problem that was found in 11.3% of patients, CSF leak was found in 2.4%, epistaxis in 1.6% while meningitis in 1.6% of the cases following Endoscopic endonasal transsphenoidal surgery for pituitary adenomas. Though, there was not any statistically significant association found among different age groups and genders for complications studied.

Keywords: Sellar lesion, CSF leak, diabetes insipidus, Endoscopic endonasal transsphenoidal surgery.

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INTRODUCTION

Pituitary adenomas, which represent around 10% of all intracranial tumors, are frequent brain tumors affecting the pituitary gland.¹ Pituitary neoplasms are considered benign tumors that mostly stem from the adenohypophysis and are divided into different categories based on their size or endocrine operation. There are two types of pituitary tumors: macroadenoma and microadenoma. According to another system of

classification, they can be either functional or non-functional adenomas, with functional adenomas being termed after the hormone they emit.²

Currently, the primary treatment surgery together with other thorough treatments is used to treat pituitary neoplasms. Endoscopic with transsphenoidal surgery, trauma tiny recognized, panoramic views are made clear, and eliminating parasellar extensions that haven't been seen under a microscope in almost 25 years. Pituitary adenomas were previously removed using microscopic transsphenoidal surgery, which has mostly been supplanted with endoscopic endonasal transsphenoidal excision of pituitary adenomas in recent years.³ Endoscopic excision of pituitary adenomas during surgery is safer and more effective than the microscopic technique.⁴ Endoscopic excision of pituitary adenomas was initially developed in the early 20th century by Harvey Cushing, and since then microsurgical transsphenoidal surgery has remained the gold standard treatment for pituitary tumors.⁵ The rationale of this study was to find early postoperative problems after endoscopic endonasal transsphenoidal surgery for the treatment of pituitary adenoma in the population of KP province. The study aimed to determine early postoperative complications of endoscopic endonasal transsphenoidal surgery for the resection of pituitary adenoma.

MATERIALS AND METHODS

Study design and setting

This Cross-sectional descriptive study was done at the Neurosurgery, PGMI Lady Reading Hospital, Peshawar from 03-02-2020 till 03-08-2020.

Sample Size

The sample size was 124 keeping a 13.4% proportion of diabetes insipidus after endoscopic endonasal transsphenoidal surgery for resection

of pituitary adenoma, 95% confidence level and 6% margin of error using the WHO calculator.

Inclusion Criteria

This study includes patients diagnosed with pituitary adenoma and focused on patients undergoing endoscopic endonasal transsphenoidal surgery for pituitary adenoma. The age bracket of patients was set between 16 – 60 years and both genders were considered in this study. The patients were from KP province and involved both educated and uneducated patients. Both positive and negative family history for carcinoma was considered and patients having BMI < 45.

Exclusion Criteria

Patients having recurrent tumors were excluded from this study. Moreover, Comorbid patients having uncontrolled diabetes mellitus (fasting blood sugar more than 126 mg/dl) and uncontrolled hypertension blood pressure more than 140/90 mm Hg, and morbid obesity (BMI > 45) patients were also excluded from this study.

Data Collection & Clinical Management

Before the commencement of this study, formal authorization was taken from the College of Physicians and Surgeons Pakistan (CPSP) and the hospital's ethical committee. The patients were incorporated through with OPD/ER department in a successive manner. Each case presented with diagnosed case of the sellar suprasellar lesion as per operational definition was registered for the study once their informed written consent had been taken. Once their complete history (disease history, its signs, and symptoms), and a complete general physical, systemic, and neurological examination were done (examination of cranial nerves and motor sensory examination) all the patients were subjected to a follow-up for seven days after surgery. During this period they were assessed for post-operative complications. Diagnosis of postoperative complications was made clinically, by laboratory tests and CT brain, like diabetes insipidus was diagnosed by laboratory tests and urine output as mentioned, epistaxis and CSF leak was diagnosed clinically, while meningitis was diagnosed clinically and confirmed by laboratory tests and CT Brain. All the information along with data related to name, age, gender, and address was recorded in a predesigned proforma.

Statistical Evaluation

The complete data was entered, processed, and evaluated using SPSS version 24.0. Descriptive statistics was used to compute mean \pm standard deviation for quantitative variables i.e. age. Frequency and percentages were presented for all qualitative variables i.e., gender, CSF leak, diabetes insipidus epistaxis, and meningitis. Immediate postoperative complications were stratified among age, and gender to see the effect of modification. Post stratification chisquare test was applied, keeping the P value \leq 0.05. All results were presented in the form of tables and graphs. Other comorbidities that will affect the results have been excluded.

RESULTS

Age and Gender Distributions

124 patients were enrolled in total. The demographic distribution of complications is given in Table 1. 56.5% (n = 70) were males with a mean age of 40.41 \pm 11.3 years and 43.5% (n = 54) were females with a mean age of 39.7 \pm 9.6 years. The cumulative mean age was 41.8 \pm 11.9 years. There were 40.3% (n = 50) of patients who were between 18 – 40 years of age and 59.7% (n = 74) were between 40 – 60 years of age.

Table 1: Distribution of patients according to gender and mean age of patients (n = 124).

Variable	Frequency	% age	Mean Age ± SD (Years)
Gender:			
Male	70	56.5	40.4 ± 11.3
Female	54	43.5	39.7± 9.6
Total	124	100	41.8 ± 11.9

Demographic Distribution of Complications

In our study, the overall study sample, 2.4% (n = 3) of patients were diagnosed to have CSF leaks as per our operational definition. The incidence of diabetes insipidus among study subjects was 11.2% (n = 14) as per our operational definition. Epistaxis was found in 1.6% (n = 2) while meningitis was also found in 1.6% (n = 2). In males, CSF leak was found to be 2.85% (n = 2) while its percentage was 1.85% (n = 1) in females. The P-value was 0.717. In the age group 16 – 40 years, CSF leak was noted in 2.0% (n = 01) while the percentage was 2.7% (n = 2) in patients in the age group 41 – 60 years. The P-value was 0.802 implicating no substantial discrepancy in CSF leak among younger and older age groups.

Endocrinological Complications

Diabetes insipidus was observed in 11.4% (n = 08) of males, and 11.1% (n = 06) of females as given in Table 2. The P-value was 0.955. In the age group 18 - 40 years, diabetes insipidus was present in 16.0% (n = 08) while the percentage was 8.1% (n = 06) in patients in the age group 41 - 60 years. The P-value was 0.173 implicating no significant difference among both age groups in diabetes insipidus. Diabetes insipidus stratification based on gender and age is given in Tables 5 and 6 respectively.

Procedural Complications

In the age group, 41 - 60 years epistaxis was

found at 1.4% (n = 1) in males and 1.8% (n = 1) in female patients with a P-value of 0.852. While meningitis was found at 1.4% (n = 1) in males and 1.8% (n = 1) in female patients with a P-value of 0.852. In the age group 16 - 40 years, Epistaxis was noted in 2.0% (n = 01) while the percentage was 1.4% (n = 1) in patients in the age group 41 -60 years. The P-value was 0.778 implicating no significant difference in CSF leak between younger and older age groups. In the age group 16 - 40 years, Meningitis was noted in 2.0% (n = 01) while the percentage was 1.4% (n = 1) in patients in the age group 41 - 60 years. The Pvalue was 0.778 implicating no significant difference in CSF leak between younger and older age groups. CSF Leak stratification based on gender and age is given in Tables 3 and 4.

Table 2: Frequency of CSF leak, Diabetes Insipidus, Epistaxis, and Meningitis in study sample according to age group (n = 124).				
Complications	Present (n/%)	Absent (n/%)		
CSF Leak	3 (2.4)	121 (97.6)		
Diabetes Insipidus	14 (11.2)	110 (88.8)		
<u>Epistaxis</u>	2 (1.6)	122 (98.4)		
Meningitis	2 (1.6)	122 (98.4)		

Table 3:	Gender vise	e stratificatior	n (CSF Leak).	
Gender	CSF L	.eak	Total	P-
Genuer	Present	Absent	Total	Value
Male	2 (2.8%)	68 (97.2%)	70 (100.0%)	
Female	1 (1.8%)	53 (98.2%)	54	0.717
Total	3 (2.4%)	121 (97.6%)	124 (100.0%)	

Table 4: Age vise stratification (CSF Leak).					
Age Group	CSF Present	Leak Absent	Total	p- Value	
16-40 Years	1 (2.0%)	49 (98.0%)	50 (100.0%)		
40-60 Years	2 (2.7%)	72 (97.3%)	74 (100.0%)	0.802	
Total	3 (2.4%)	121 97.6%)	124 (100.0%)		

Table 5: Gender vise stratification (diabetes insipidus).

Canadan	Diabetes Insipidus		Tatal	p-
Gender	Present	Absent	lotal	Value
Male	8 (11.4%)	62 (88.6%)	70 (100.0%)	
Female	6 (11.1%)	48 (88.9%)	54 (100.0%)	0.955
Total	14 (11.2%)	110 (88.8%)	124 (100.0%)	

Table 6: Ag	Table 6: Age vise stratification (diabetes insipidus).					
Age Group	Diabetes Present	Insipidus Absent	Total	p- Value		
16 – 40 Years	08 (16.0%)	42 (84%)	50 (100.0%)			
40 – 60 Years	06 (08.1%)	68 (83.9%)	74 (100.0%)	0.173		
Total	14 (11.2%)	110 (88.8%)	124 (100.0%)			

Table 7: Gender vise stratification (Epistaxis).					
Gender	Ep Present	istaxis Absent	Total	p- Value	
Male	01 (1.4%)	69 (98.6%)	70 (100.0%)		
Female	01 (1.8%)	53 (98.2%)	54 (100.0%)	0.852	
Total	03 (2.4%)	121 (97.6%)	124 (100.0%)		

Table 8: Gender vise stratification (Meningitis).

Condon	Meningitis		Total	p-
Gender	Present	Absent	Total	Value
Male	01 (1.4%)	69 (98.6%)	70 (100.0%)	
Female	01 (1.8%)	53 (98.2%)	54 (100.0%)	0.852
Total	03 (2.4%)	121 (97.6%)	124 100.0%)	

Table 9: Age-wise stratification of Epistaxis.

Age Epistaxis		istaxis		P-
Group	Present	Absent	Total	Value
16 – 40 Years	01 (02%)	49 (98%)	50 (100.0%)	
40 – 60 Years	01 (1.4%)	73 (98.6%)	74 (100.0%)	0.778
Total	02 (1.6%)	122 (98.4%)	124 (100.0%)	

Table 10: Age-wise stratification of Meningitis.					
Age Group	Men	ingitis	Total	P- Value	
	Present	Absent		value	
16 – 40 Years	01 (02%)	49 (98%)	50 (100.0%)		
40 – 60 Years	01 (1.4%)	73 (98.6%)	74 (100.0%)	0.778	
Total	02 (1.6%)	122 (98.4%)	124 (100.0%)		

DISCUSSION

About 10 – 15% of all primary brain cancers are pituitary adenomas, and about one-third of pituitary adenomas are clinically non-functioning pituitary adenomas (NFPA). Most of these tumors are mega adenomas when they are diagnosed, and clinical manifestations emerge from the surrounding structures being compressed, hence Hypopituitarism, headache, visual abnormalities, and oculomotor symptoms are next palsy. Surgery is considered the key preliminary therapy for NFPA, and the objectives of care involve the total excision of the pituitary tumor to prevent a recurrence, treat hormonal imbalances, and decompress the nervous system. Endoscopic endonasal pituitary surgery was first reported by Jho et al⁶ and then turn out to be frequent. Compared to the microscopic transsphenoidal endoscopic method, the endonasal transsphenoidal approach (eTSS) provides greater access to the skull base and more panoramic visibility (mTSS).⁷ The usage of eTSS has expanded thanks to technological developments endoscopes, such angled specialized as equipment, and image guide. According to reports, this procedure increases resection rates, causes fewer problems, and returns hormone levels to normal ranges. The overall gross total tumor removal rate for NFPA patients who undergo surgery using eTSS is 75.2 - 93% 147, 148, 149, which is higher than the rate for patients who undergo surgery using mTSS (as technology advances, more and more techniques are being developed for wider angles

and increased procedure safety). Hide et al, reported that 26 patients with pituitary adenomas undertook endoscopic endonasal transsphenoidal surgery while wearing an indocyanine green endoscope(2). This meant that the patients received a bolus injection of 12.5 mg of indocyanine green into a peripheral vein and observed the internal carotid arteries, cavernous inter-cavernous sinus, and pituitary. sinus, Additionally, the endoscopy and pictures are in dimensions. During the endoscopic three endonasal transsphenoidal surgery, guidance was reported. Ishikawa Mami et al. described employing endonasal ultrasound in the neuroendoscopic Transsphenoidal surgerv has demonstrated its value as a real-time monitoring procedure, and dynamic pictures safeguarding method).

The rationale of the study was to determine postoperative complications the early of endoscopic endonasal surgery for the treatment of pituitary adenoma in our population. So far there is no study focusing on this topic in our population. As this is the most common site of primary brain tumors and is difficult to resect due to its proximity to vital structures such as the optic nerve and carotid arteries. This study will show the magnitude of patients undergoing pituitary adenoma and as endoscopic endonasal transsphenoidal surgery is the procedure of choice for these tumors, its complications are important to be known in our population. Furthermore, no work is done on this topic regarding our population. My study will provide accurate and relevant data for the identification and prevalence of early postoperative complications of endoscopic endonasal transsphenoidal surgery for pituitary adenoma. This data will be used for further research work and recommendations for improving skills and better management of patients with this tumor for a better outcome. As this data will be collected from our population, it will be more reliable and applicable to our population.

The light of recommendations made based on my data will provide better care to patients and good outcomes for these complications. A total of one hundred and twenty-four (n = 124) patients were recruited in this study. Patients between the ages 16-60 years, irrespective of gender, who were diagnosed with cases of pituitary adenoma operated by EETS with a BMI < 45 were included in the study.

Patients having recurrent tumors, re-do cases, and patients having comorbid conditions like patients with uncontrolled diabetes, hypertension, and morbid obesity with BMI > 45 were omitted from this research. Records were obtained using a designed proforma. 56.5% of patients were male with a mean age of 40 years and 43.5% of patients were females with a mean age of 39 years. The cumulative mean age was 41.8 years. There 40.3% of patients were between 18 - 40 years of age and 59.7% were between 40 – 60 years of age. We studied the CSF leak, the incidence of diabetes insipidus, epistaxis, and meningitis in the study as a postoperative complication following EETS surgery for pituitary adenoma. The overall incidence of CSF was found to be 2.4% among the total study population, while diabetes insipidus was noted in 11.2% of the study population. Epistaxis was found in 1.6% while meningitis was also found in 1.6%. Moreover, it was found that the CSF leak was reduced amount in females at 1.8% as compared to males at 2.8%. Though, the results were not statistically substantial as the P-value was 0.717. On contrary, CSF leak was more frequently seen in patients more than 40 years of age which was 2.7% while 2.0% in the age group less than 40, the p-value was 0.802. In our study, the incidence of diabetes insipidus was higher in males at 11.4% as compared to females at 11.1% (P-value: 0.955). Contrary to the CSF leak, the diabetes insipidus was more frequently reported in ages less than 40 years of age which was 16.0% while 8.1% (P-value: 0.173). While epistaxis was found at 1.4% in males and 1.8% in female patients (P-value: 0.852).

While meningitis was found at 1.4% (n = 1) in males and 1.8% (n = 1) in female patients (P-value: 0.852).

Our results are consistent with already published data. a retrospective study of around 109 consecutive cases of pathology was done by Lin et al, with validated Roethke's cleft cysts treated transsphenoidal (RCCs) using а methodology during a period of 20 years (1995 to 2016).8 This study comprises 109 surgeries in 100 patients, and an average follow-up period of 67 months (range of 3 - 220 months). The mean of patient age involved in this study was around 44.6 years (age range of 12 - 82 years), and out of these cases, 73% were female. The mean diameter of the maximal cyst was 14.7 mm. In 53% of cases under study, intraoperative CSF leak fixation was carried out and it was found frequent in reoperation cases (71% vs. 48%, p < 0.001). No other neurological shortfalls or perioperative deaths were observed. Around 1.8% (2 patients) were also found to develop postoperative CSF leaks. Diabetes insipidus (DI) development was also identified in these cases with Transient Diabetes insipidus developed in 22% of the patients (24 cases) and permanent DI in 5.5% (6 cases). In 6.4% (7 cases) delayed postoperative hyponatremia also progressed. Of the 66 patients who had a preoperative headache, postoperative improvement 42.2% (28 cases) of 61 reported and 57.8% (38) reported no change. Lin M et al, established in their study that TSS surgery for RCCs is a reliable and useful mediation for symptomatic lesions. They also commented that though it is an effective methodology, full RCC excision is in general not suggested as it is associated with the risk of hypopituitarism, DI, and CSF leaks.

Butenschoen et al evaluated the cases that dealt with the treatment of pituitary adenoma during a period of around 13 years (2006 to 2019) at the Department of Neurosurgery, Technical University Munich, Germany.⁹ The pituitary function was evaluated pre- and post-operation and at 6 weeks to 12 weeks as well as at 1-year follow-up. This study included 211 patients. Just about 9% of the patients recovered from preoperative adrenal insufficiency while 10.4% of the patients were found to develop hormone therapy need. It was also observed that postoperative dawn cortisol concentrations were to a lesser extent sensitive and particular in calculating long-term corticotroph function compared to amounts measured after 6 weeks and 1 year, highlighting the significance of endocrine follow-up testing.

Chatzidakis et al, designed research to get an insight into the post-operative effects of initial cases conducted by a group of two young surgeons employing the EET methodology, in comparison to the cases handled by a team of experienced senior neurosurgeons in MST approach.¹⁰ Records of 20 patients with pituitary adenoma were compared from one center who were operated by both teams. All the patients in the EET group presented with visual impairment recovered completely (5/5), while 80% of the cases in the MST group undergo complete recovery (80%). The primary hospitalization period was parallel in either group. Gross tumor removal was accomplished in 90% of patients in the EET group while it was 70% in the patients with MST operated on the procedure. Intraoperative complications were found fairly equivalent in these groups. The initial cases operated at the center with EET demonstrated improved visual effects and greater tumor elimination in comparison to the MST group. A better understanding of employing this procedure could exponentiate the discrepancies in the post-operative effects including decreased hospitalization period and a small number of intraoperative impediments. Chatzidakis, based on their findings, suggested that the endonasal endoscopic methodology for pituitary tumors has the propensity to be recognized as the gold standard technique, based on progressively

growing ground over the traditional microscopic approach.

Rutland et al conducted an interesting study by reviewing the medical history of around 587 undertook patients who endoscopic transsphenoidal surgery at the Mount Sinai Medical Centre from January 2013 to August 2018.¹¹ It targeted and analyzed the cases undergoing post-operative vision weakening, characterized by lowered visual perception, exacerbated VFDs, or new onset of blurry vision. They found that 11 patients out of the total, who underwent endoscopic surgery for pituitary adenoma showed post-operative vision impairment. Out of these, 7 patients underwent visual impairment within 24 hours of surgery. Elevated graft placement (10 out of 11 patients) and opening of the diaphragma sellae (9 out of 11 patients) were also found in this series.

Huo et al conducted a comparison regarding the prevalence of post-op CSF leak between two groups, one with upfront LD insertion and the other without it.¹² This was a monitored trial study organized over 5 years with cases experiencing extended endoscopic trans-sphenoidal surgery arbitrarily assigned to either LD insertion at the time of surgery, or without it. 38 patients from three tertiary hospitals in Melbourne with anterior skull base tumors were considered in this study. No substantial disparity in post-op CSF leak incidence was observed between the two subgroups (12.50% in the LD arm vs. 9.10% in the no LD arm). While the patients with LD insertion showed significantly high complication rates, lengthier hospital stays, and reduced subjective quality of life measures at 12 months in comparison to those without LD.

Akins et al worked on identifying the complications in a series of open and endoscopic complex skull base and craniofacial surgery and assess it in comparison with their institutional database for craniotomy (13). Acute complications were observed in 38% of patients while delayed complications were found in 17%.

In contrast, to the group official craniotomy database (n = 2143), complex skull base surgery had higher rates for motor deficit 1.7% vs 6.7% and that of encephalopathy was 1.4% vs. 6.7% while CSF leak was 0.7% vs. 13.3%.

In summary, EETSS is a reliable and efficient mode of surgery for pituitary adenomas with little trauma and lesser perioperative complications. The studies quoted here reported adequate surgical outcomes with minimal rates of morbidity and mortality. Earlier microscopic transsphenoidal surgery was employed for the resection of pituitary adenomas which is now replaced mostly by endoscopic endonasal transsphenoidal resection of pituitary adenomas. Despite excellent results over all these years, EETSS has been associated with a few complications. These include CSF leak, diabetes insipidus, epistaxis, and meningitis, which are described by several studies common complications amongst them as diabetes insipidus are the most common immediate postoperative complication. But these complications can be treated successfully and can be avoided to some extent using modern tools for EETSS like carotid Doppler and indomethacin green. Diabetes insipidus and CSF leak have been described in various studies but very few studies have described epistaxis and meningitis as immediate post-operative complications of EETSS, moreover, no study has yet been done on this topic for the population of KP province.

My study will provide accurate and relevant data for the identification and prevalence of early postoperative complications of endoscopic endonasal transsphenoidal surgery for pituitary adenoma, but the limitation of this study is that it has been done on a very small population as well as the very limited proportion of the overall country population has been included in the study. This data will be used for further research provide recommendations work and for improving skills and better management of patients with these complications after EETSS for pituitary adenomas for a better outcome. As this

data is collected from our population, it will be more reliable and applicable to the KP population.

CONCLUSION

Diabetes insipidus is a more frequent early postoperative complication which was found in 11.3% of patients, CSF leak was observed in 2.4%, Epistaxis in 1.6% while meningitis in 1.6% of patients following Endoscopic endonasal transsphenoidal surgery for pituitary adenomas. However, no statistically significant association was found among different age groups and gender for all these complications.

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Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:	
1.	Taimoor Ali	1. Study design, data collection and calculations.	
4.	Taimoor Ali&Arshad Iqbal	4. Analysis of data and interpretation of results.	
5.	Arshad Iqbal	5. Literature review and referencing.	
6.	Usman Haqqani	6. Editing and quality insurer.	

AUTHORS CONTRIBUTIONS

Additional Information

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Conflicts 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 relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

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