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Clinical and Radiological Outcomes of Endoscopic Endonasal Transsphenoidal Surgery for Pituitary Adenomas

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ABSTRACT

Background: Pituitary adenomas may cause problems because of hormonal hypersecretion, pituitary hormonal failure, vision loss, headaches and/or bleeding into the tumor (apoplexy).

Objectives: The purpose of this study was to evaluate the efficacy of the endoscopic endonasal approach in managing pituitary adenoma concerning the resection rate and other clinical outcomes. Also, to assess the safety of the approach.

Patients and methods: A prospective cohort study was conducted on twenty-four patients undergoing endonasal transsphenoidal approaches for pituitary adenomas at the Department of Neurosurgery, Zagazig University Hospitals during the period from March 2022 to October 2022. All patients were subjected to complete clinical examination, hormonal assessment, and neuroimaging.

Results: This study demonstrated that among cases with hypopituitarism (66.7% became normal after treatment and 33.3% remained suffering from hypopituitarism) with statistically significant difference between pre & post treatment ($p=0.03$). For cases with normalized hormonal level pre-operative change to 5 cases hypopituitarism (4 transient diabetes insipidus and one case permanent Diabetes insipidus at one or more axis) and 13 cases remained normalized with statistically significant difference between them ($p<0.001$). All cases of increased GH, ACTH and prolactin showed complete improvement after treatment and 90% of prolactinoma improved after treatment.

Conclusion: It could be concluded that the minimally invasive endoscopic endonasal transsphenoidal approach is an effective and safe approach for the management of pituitary adenomas.

Keywords: Pituitary Adenomas, Endoscopic, Endonasal

INTRODUCTION

Pituitary adenomas are benign clonal neoplasms of the neuroendocrine epithelial cells of the adenohypophysis. It is considered the most common type of pituitary disorder [(1)]. It accounts for 10-15% of all intracranial masses [(2)].

Pituitary adenomas are classified by size and whether they produce pituitary hormones, microadenomas are less than 1 cm in diameter and macroadenomas are over 1 cm in diameter [(3)].

Pituitary adenomas may cause problems because of hormonal hypersecretion, pituitary hormonal failure, vision loss, headaches and/or bleeding into the tumor (apoplexy) [(4)].

Endocrine-active adenomas that make excess hormones (endocrine-active adenomas) include prolactin-secreting adenomas known as prolactinomas, adrenocorticotropic hormone (ACTH) secreting adenomas causing Cushing's disease, growth hormone (GH) secreting adenomas causing acromegaly, and thyroid stimulating hormone (TSH) secreting adenomas causing hyperthyroidism. Endocrine-inactive Adenoma Adenomas that do not make excess hormones are called endocrine-inactive or Non-Functional Adenomas [(5)].

Pituitary hormonal deficiency (Hypopituitarism) typically occurs only in larger tumors (macroadenomas) and results from compression and damage to the normal pituitary gland from the enlarging adenoma [(6)].

Bleeding (pituitary apoplexy) develops over hours to several days from hemorrhage and/or infarction of pituitary adenoma (typically a macroadenoma). Symptoms may include Headache, Nausea, Visual loss, Double vision and Confusion.

Pituitary adenomas are best diagnosed by imaging studies and hormonal testing. The imaging study of choice is an MRI of the pituitary gland without and with gadolinium (a contrast agent). A brain MRI or CT scan paranasal will also reveal most pituitary macroadenomas but may not reveal smaller microadenomas. Beside imaging there is Pituitary Hormonal Testing, Evaluation, and interpretation of the pituitary gland function either for hormonal deficits or inappropriate hormonal secretion is performed full hormonal profile. Also, Neuro-Ophthalmological Evaluation Patients with visual complaints or those whose tumors that contact the optic nerves or optic chiasm should receive a full ophthalmological evaluation. An evaluation with our neuro-ophthalmologist should include acuity (vision quality) testing of each eye and formal visual field testing to determine if there is loss of peripheral vision [(2,7)].

This study was aimed to evaluate the efficacy of the endoscopic endonasal approach in managing pituitary adenoma concerning the resection rate and other clinical outcomes. Also, to assess the safety of the approach.

PATIENTS AND METHODS

This prospective cohort study included a total of twenty-four patients undergoing endonasal transsphenoidal approaches for pituitary adenomas,

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attending at Department of Neurosurgery with the incorporation of an otolaryngologist, Zagazig University Hospitals. This study was conducted between March 2022 and October 2022. Eleven patients (45.8%) were males and thirteen (54.2%) were females.

Inclusion criteria: Patients who were fit and eligible to be operated transsphenoidal. All ages and both sexes. Patients diagnosed with pituitary adenoma that had been demonstrated and confirmed with pathology-confirmed PA and magnetic resonance imaging (MRI).

Exclusion criteria: Patients not suitable for endoscopic endonasal excision. Patient's lesions not available to the endoscopic excision, and eligible for transcranial microscopic excision. Patients with large pituitary adenomas and lies on faraway our field, recurrent giant adenomas, ectatic 'kissing' carotids, vascular lesions as AVM and aneurysm and patients who didn't complete their follow up.

Preoperative investigations:

All patients were subjected to demographic data taking, complete clinical examination included general, neurological, and endocrinological examinations. Complete hormonal assessments of the patients on their admission were done including serum prolactin level, serum ACTH and cortisol levels, serum GH and IGF-1 levels in Acromegalic, serum T4 and TSH and serum FSH, LH and testosterone level according to sex. These hormonal assessments were repeated on the third week and three months later during the follow up. Computerized tomography (CT) was performed on both brain and paranasal sinuses. MRI brain (sellar protocol) dynamic post contrast was performed. **Laboratory investigations**: full routine lab evaluation was done in the form of complete blood count (CBC), liver and kidney function tests, blood sugar, serum sodium and potassium, and coagulation profile.

Surgical Management:

All patients were given pre-operative steroids (100 mg hydrocortisone) stress dose as prophylaxis, and one gram of a third-generation cephalosporin was given intravenously after induction of anesthesia and continued in the postoperative period. As a drip during surgery, A folly's catheter was applied to all patients before surgery and for one night after surgery to monitor the possibility of diabetes insipidus. The patients were anaesthetized with orotracheal intubation. The eyes were protected with an application of ophthalmic ointment and covered with soft vinyl adhesives.

The oropharyngeal cavity is packed with a 2-inch-wide roll of gauze, and the end of the roll is clamped using an artery forceps to avoid missing removal at the end of surgery. The face and nasal cavity are then prepared with 5% povidone –iodine solution. The patient, C-arm fluoroscopy, and endoscopic video camera equipment are then drapped following aseptic techniques.

Post-operative:

All patients postoperatively were transferred to the intensive care unit. Patients were continued on the same third generation cephalosporin intravenously for three days unless CSF leak, infection, or wound collection was noticed in such cases antibiotics were continued. Steroids were also given in gradual tapering doses. Patients receiving preoperative hormone supplementation were continued on them post operatively. Urine output was recorded and an input and output chart were documented. Regular check of serum electrolytes was performed.

Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. Written informed consent was taken from all participants. The study was conducted according to the Declaration of Helsinki.

Statistical analysis

All data was collected, tabulated and statistically analyzed using SPSS software, version 18 (SPSS Inc., PASW statistics for windows version 18. Chicago: SPSS Inc.). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for non-normally distributed data and mean± Standard deviation for normally distributed data after testing normality using Shapiro Wilk test. Significance of the obtained results was judged at the (0.05) level. Chi-Square, Fischer exact test, Monte Carlo tests were used to compare qualitative data between groups as appropriate. Marginal Homogenity test (Stewart Maxwell) was used to compare qualitative data pre and post –treatment. Binary logistic regression was used to assess the effect of combination of more than 2 independent variables on dichotomous outcome using Stepwise / forward Wald / Enter technique.

RESULTS

Table (1) shows that the mean age of the studied cases was 43.58±5.32 years ranging from 30 to 52 years, 70.7% aged more than or equal to 40 years, 54.2% are females.

Table (1): Demographic characteristics of the studied cases

Variable (No.=24)		No.	%
Age /years	**Mean ±SD (min-max)**	43.58±5.32 (30-52)	
Age groups	**≤40**	7	29.2
	>40	17	70.8
Sex	**Male**	11	45.8
	Female	13	54.2

Table (2) illustrates that 91.7% of the studied cases had visual disturbance with mean duration 3.68 months, 50% menstrual disturbance with mean duration 21.17 months, 45.8% sexual dysfunction with mean duration 8.73 months, 25% hypopituitarism with mean duration 8.73 months, 8.3% acromegaly with mean duration 15 months, 4.2% Ophthalmoplegia with duration 3 weeks & 4.2% Cushing disease with duration 12 months.

Table (2): Clinical presentation of patients and their duration:

Variable (No.=24)		No.	%	duration /months
Clinical presentation	Visual disturbance	22	91.7	3.68±0.99 (3-6)
	Menstrual disturbance, Galactorrhea	12	50.0	21.17±11.89 (6-36)
	Ophthalmo-plegia	1	4.2	3weeks
	Acromegaly	2	8.3	15.0±12.7 (6-24)
	Cushing disease	1	4.2	12
	Sexual dysfunction	11	45.8	8.73±2.83 (3-12)
	Hypopituitarism	6	25.0	14.83±9.62 (3-30)

Table (3) shows that there was statistically significant improvement of visual disturbance symptoms. Pre-operative visual symptoms is distributed as following; 15 eyes incomplete hemianopia, 11 eyes complete hemianopia, 14 eyes central blind spot enlarged scotoma and 4 eyes severe loss. Complete hemianopia & severe loss significantly improved after treatment from (11 to 8 eyes and 4 to 0 eyes, respectively).

Table (3): Visual disturbance of the studied patients

Visual disturbance (No.=44 eyes)	Pre-operative		Post-operative		Stuart Maxwell test
	No.	%	No.	%	
Incomplete hemianopia	15	34.1	15	34.1	p=0.01*
Complete hemianopia	11	25.0	8	18.2	
Central blind spot enlarged scotoma	14	31.8	14	31.8	
Severe loss	4	9.1	0	0	
Normal	0	0	7	14.6	

*statistically significant

Table (4) shows that 83.4% macro tumor size, 8.3% micro, macro with cavernous invasion. All cases with microadenoma and macro with Cavernous invasion have complete excision and 90% of cases with macroadenoma are completely excised.

Table (4): Tumor size of patients and their duration.

Tumor size	No.	%	Operative intervention (Complete excision)
Micro	2	8.3	2(100%)
Macro	20	83.4	18(90%)
Macro with Cavernous invasion	2	8.3	2(100%)

Table (5) demonstrates that; 50% of the studied cases have prolactinoma, 37.5% nonfunctioning adenoma, 8.3% Growth hormone secreting adenoma, 4.2% ACTH - secreting adenoma.

Table (5): Different types of hormonal disturbances in pituitary adenomas

Variable (No.=24)		No.	%
Hormonal typing	Prolactinoma	12	50
	Non-functioning	9	37.5
	GH - secreting adenoma	2	8.3
	ACTH - secreting adenoma	1	4.2

Table (6) demonstrates that 22 cases (91.7%) of the studied cases have totally removed adenoma and 2 cases (8.3%) residual.

Table (6): MRI findings of the studied cases

		n=24	%
MRI follow up	Totally removed	22	91.7
	Residual	2	8.3

Table (7) demonstrates that among cases with Hypopituitarism (66.7% become normal after treatment and 33.3% still hypopituitarism) with statistically significant difference between pre & post treatment (p=0.03).

For cases with normalized hormonal level pre-operative change to 5 cases hypopituitarism (4 transient diabetes insipidus and one case permanent Diabetes insipidus at one or more axis) and 13 cases remain normalized with statistically significant difference between them (p<0.001).

Table (7): Hormonal improvement between pre and post-operative treatment.

Hormonal Typing	Pre n=24(%)	Post n=24(%)	P Value
Hypopituitarism	6	2(33.3)	0.03*
Normalized	0	4(66.7)	
Normalized	18	13(72.2)	0.01*
Hypopituitarism	0	5(27.8)	

Used test :MC-Nemar test , *statistically significant

Table (8) shows that all cases of increased GH, ACTH and prolactinoma show complete improvement after treatment and 90% of prolactinoma improved after treatment.

Table (8): Improvement of prolactinoma, ACTH & growth hormone

Improvement	Number	Number of complications	% Of improvement
Prolactinoma	12	2	90.0%
GH	2	0	100.0%
ACTH	1	0	100.0%

DISCUSSION

The present results showed that the mean age of the studied cases was 43.58±5.32 years ranging from 30 to 52 years, 70.7% aged more than or equal to 40 years, and 54.2% were females.

Our results were in accordance with **Thotakura *et al.*** in their study on one hundred consecutive patients of pituitary adenomas with SSE operated by trans-sphenoidal approach. Of the 100 patients, 52 were males, and 48 were females. Age range was 14-74 years with a mean of 42.47 ± 1.32 years[(8)].

Regarding clinical presentation in our results, 91.7% of the studied cases had visual disturbance with mean duration 3.68 months, 50% menstrual disturbance with mean duration 21.17 months, 45.8% sexual dysfunction with mean duration 8.73 months, 25% hypopituitarism with mean duration 8.73 months, 8.3% acromegaly with mean duration 15 months, 4.2% Ophthalmoplegia with duration 3 weeks & 4.2% Cushing disease with duration 12 months.

Thakur *et al.* reported that regarding clinical presentation and surgical indications in 514 patients, 215 cases had hypopituitarism, 209 had endocrine-active adenoma, 145 cases had vision field or acuity deficit, and 132 had headaches[(9)].

Our results agreed with **Thakur *et al.*** who reported that the most common surgical indications and clinical presentations included hypopituitarism 58 (47%), vision loss 48 (39%),tumor growth on serial imaging 23 (18.7%) and chiasmal compression 21 (17%). Eleven (8.9%) patients had asymptomatic macroadenomas (mean maximal tumor diameter 17.7 ± 5.6 mm) associated with gland compression but normal gland function and opted for surgery. Overall, 35 (28%) patients were discovered as incidental findings. Of these, there were 20 patients who complained of headaches [(9)].

The present study was agreed with **Castle-Kirszbaum *et al.*** who reported that of the 304 pituitary adenomas, 116 (116/304, 38.2%) were functional. Of these, there were 43 cases (43/116, 37.1%) of acromegaly, 50 cases (50/116, 43.1%) of Cushing's disease, 18 cases (18/116, 15.5%) of prolactinoma, 2 TSHomas (2/116, 1.7%) and 3 co-secretory tumors (2/116, 2.6%) (2 co-secreted GH and PRL, the other ACTH and PRL). Of the 188 (188/304, 61.98%) non-functional adenomas, 72.3% (137/188) had normal preoperative endocrine function[(9)].

As regard visual disturbances, there was statistically significant improvement of visual disturbance symptoms. Pre-operative visual symptoms is distributed as following ; 15 eyes incomplete hemianopia, 11 eyes complete hemianopia, 14 eyes central blind spot enlarged scotoma and 4 eyes severe loss . Complete hemianopia & severe loss significantly improved after treatment from (11 to 8 eyes and 4 to 0 eyes, respectively).

The current study was in line with **Thotakura *et al.*** who revealed that there were 71 patients with preoperative visual impairment. Vision improved in 61 of the 71 patients (85.91%). Vision was normalized in 31 patients. Vision remained same in 6 patients and deteriorated in 1 patient. Among the 71 patients who had preoperative visual impairment, only 66 patients had visual symptoms, and the rest had occult deficits. The mean duration of visual symptoms is 11.77 (0.15-100) months. Thirty-eight patients had visual symptoms of < 1-year duration and 25 patients had visual symptoms more than or equal to 1-year duration. Postoperatively 1 patient died with myocardial infarction [(8)].

Our findings were agreed with **Thakur *et al.*** they revealed that of 48 (46%) patients with preoperative visual field or acuity decline, complete resolution, improvement, stability, or visual worsening occurred in 11 (23%), 31 (64.5%), 5 (10.4%) and 1 (2%), respectively[(9)].

Castle-Kirszbaum *et al.* one third of pituitary adenomas (102/304, 33.6%) had a preoperative visual field deficit, mostly complete (32/102, 31.4%) or incomplete (52/102, 51.0%) bitemporal hemianopias. Monocular field defects, representing prechiasmatic compression, were seen in 14.7% (15/102) of cases, while homonymous field cuts, representing postchiasmatic compression, were rare (3/102, 2.9%). Only two patients (2/304, 0.7%) had visual field worsening after surgery, while 71.6% (73/102) experienced partial or complete resolution of their field cut after surgery. Preoperative ophthalmoplegia was seen in seven (7/304, 2.3%) adenomas, three of these in the context of apoplexy. Four of these (4/7, 57.1%)

recovered with surgery, but 3 (3/304, 1.0%) new cases of cranial neuropathy occurred (two involving the oculomotor nerve and one involving the abducens nerve) [(10)].

Our findings revealed that 83.4% macro tumor size, 8.3% micro, macro with cavernous invasion. All cases with microadenoma and macro with Cavernous invasion have complete excision and 90% of cases with macroadenoma are completely excised.

Osman *et al.* reported that 80 cases (80.8%) were marcroadenoma (> 1cm), while 8 cases (8.1%) were microadenoma (<1cm) and 11 cases (11.1%) were giant adenomas (> 4cm) [(11)].

The present study was agreed with **Wang *et al.*** who reported that regarding the tumor size they have stratified the tumor size into 3 grades, 4.9% were <10 mm, 88.9% were between 10-40 mm, and 6.2% were >40 mm[(12)].

Respecting types of hormonal disturbances in pituitary adenomas in the current study, 50% of the studied cases have prolactinoma, 37.5% non-functioning adenoma, 8.3% Growth hormone secreting adenoma, 4.2% ACTH - secreting adenoma.

The current study was in line with **Wang *et al.*** reported that regarding the types of adenoma, 55.6% were non-functioning adenoma, 22.2% were prolactinoma, and 22.2% were gonadtropinoma[(12)].

Thakur *et al.* reported that 59.3% had non-functioning adenoma, and 40.7% had endocrine active adenoma. 18.6% had Cushing disease, 10.9% had acromegaly, 12.6% had prolactinoma, 0.5% had TSH-secreting adenoma, and 0.5% had mixed GH-prolactin or GH-TSH secreting adenomas[(9)].

Our findings were agreed with **Thakur *et al.*** reported that 468 patients operated on for pituitary adenoma, 123 (26%) were ≥ 65 years (range 65–93 years); 106 (86.2%) had endocrine-inactive adenomas; 18 (14.6%) had prior surgery. Of 106 patients with endocrine-inactive adenomas, gross total resection (GTR) was achieved in 70/106 (66%). Of 17 patients with endocrine-active adenomas, early biochemical remission was: Cushing's 6/8; acromegaly 1/4; prolactinomas 1/5[(9)].

Our results were in accordance with **Castle-Kirszbaum *et al.*** reported that Over half the cases (60.9%) were non-functioning (NFPA), while of the functional tumours, GH (14.1%) and ACTH (16.4%), TSH (1%), prolactinoma (5.9%), and co-secreting (1.6%)[(13)].

MRI findings in the current study demonstrated that 22 cases (91.7%) of the studied cases have totally removed adenoma and two cases (8.3%) residual.

Wang *et al.* reported that regarding tumor resection, 58% were completely resected, 28.4% were massively resected, and 13.6% were partially resected[(12)].

Benveniste *et al.* found repeat transsphenoidal surgery to be a safe and effective treatment option in their series of 96 patients who had recurrent or residual pituitary adenoma [(14)].

The current study was in line with **Luomaranta *et al.*** found that of the 37 patients with a preoperative visual pathway of pituitary adenoma (VP-PA) contact, 32 (86.5 %) had no tumor remnants in contact with their VP on their postoperative MRIs. In addition, three patients (8.1 %) had just a small tumor remnant touching their VP, without any displacement or compression. However, two patients postoperatively still proved to have displaced VPs by the residual tumor; one (2.7 %) with less than one-third and another (2.7 %) with more than two-thirds of their preoperative VP displacements [(15)].

The Hormonal improvement between pre and post-operative treatment in our study demonstrated that among cases with Hypopituitarism (66.7% become normal after treatment and 33.3% still hypopituitarism) with statistically significant difference between pre & post treatment (p=0.03). For cases with normalized hormonal level pre-operative change to 5 cases hypopituitarism (4 transient diabetes insipidus and one case permanent Diabetes insipidus at one or more axis) and 13 cases remain normalized with statistically significant difference between them (p<0.001).

Wang *et al.* reported that the proportion of patients with hypopituitarism increased to 44.4% and 45.7% at postoperative days 1 and 7, respectively and then went down to 23.5% at 4 months follow-up. However, these changes did not reach statistical significance[(12)]. There results were in line with our results but there was significant difference between pre- and post-operative regarding hypopituitarism.

CONCLUSION

It could be concluded that the minimally invasive endoscopic endonasal transsphenoidal approach is an effective and safe approach for the management of pituitary adenomas regarding resection rate, and clinical outcome.

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