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ORIGINAL ARTICLE

Long Term Post-Treatment Follow-Up of Pituitary Tumours

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ABSTRACT

Aim: To study the spectrum of Pituitary tumours, their presentation, treatment and compliance with follow-up.
Study design: Mixed retrospective and prospective study
Place and duration of study: Medicell Institute of Diabetes, Endocrinology and Metabolism and Jinnah Postgraduate Medical Centre Karachi from 1st January 2012 to 31st July 2022.
Methodology: One hundred and seventy three cases of pituitary tumours, were enrolled. Data regarding age, gender, duration of disease, symptoms, mode of treatment administered and compliance with the follow-up instructions was retrieved.
Results: The mean age was 36.4±10.6 years. Female predominance was seen in 97(56.1%). Of the 136 married patients, subfertility was seen in 48(36.3%). Headache was observed in 164(94.8%) of patients. Prolactinoma was the lead tumour comprising of 76 cases (43.9%), followed by non-secretory tumours 47(27.2%), and acromegaly 43(24.9%). Other rare disorders including Cushing's disease, craniopharyngioma and gonadotropinoma were also seen. Cabergoline was prescribed in 136 (78.6%) cases. Transsphenoidal surgery (TSS) was done in 74(42.8%) of patients. Out of 97 female patients, 38(39.2%) had persistent amenorrhea post-treatment, while this data was not available for 40(41.2%) of these women, who were lost to follow-up. The difference between mean prolactin levels prior and after the treatment (1390.048±2646.986 versus 116.360±163.369) were found to be statistically significant p<0.001). Similarly, IGF-1 levels were significantly improved post treatment indicating tumour stability. Moreover, the level of mean FT4 post-treatment was 1.64, reflecting adequate replacement.
Conclusion: Majority of the patients had improvement post-treatment in pituitary tumour symptoms including vision, headache and sexual function. Failure to attend for follow-up for tumour stability, control of excess hormone, and pituitary hormone replacement was seen in a large number of patients in this study. This requires careful consideration of different strategies to ensure better long term care in pituitary tumours.
Keywords: Pituitary tumor, Prolactinoma, Craniopharyngioma, Gonadotropinoma, Acromegaly

INTRODUCTION

Prolactin, growth hormone, and adrenocorticotropic hormone are commonly over secreted by pituitary adenomas (PA). Follicle-stimulating hormone (FSH), luteinizing hormone (LH), and thyroid stimulating hormone (TSH) are far less common[1,2]. Most PAs are harmless, but about 0.1% to 0.2% of them are malignant[3]. The more cancerous a PA is, the worse its prognosis[4]. Symptoms of endocrine problems and tissue compression within the pituitary and the surrounding structures due to the expanding tumour are the most common clinical signs of PAs. The treating PA is to relieve pressure on the patient's nervous system, preserve nerve function, restore metabolic and hormonal balance, and enhance the patient's quality of life[5].

Patients treated for pituitary adenomas have benefited greatly from the advancement of surgical methods and medical therapy. Transsphenoidal (TSS) pituitary surgery with access to the pituitary gland through the endonasal corridor has proven to be highly successful in treating pituitary tumours. It has significantly lower postoperative complications as opposed to transcranial surgery. Quality of life (QoL) indicators have also been developed specifically for various pituitary tumours in evaluating the efficacy of therapy[6-8]. It is important to be aware of the potential for complications after a PA resection. Hypopituitarism, for instance, affects 3.6-13.6% of individuals after PA resection.[9] Patients with hypopituitarism can have a wide range of symptoms, from indifference and lethargy to a fuzzy state of mind to potentially life-threatening ones like coma. Fatigue, impotence, sleep disturbances, disturbance of vision, changes in appearance, feeling of melancholy, and anxiety are only some of the pre-existing symptoms that persist for many PA patients after tumour removal[10,11].

The purpose of this study was to assess the long term post treatment follow-up of Pituitary tumours in terms of control of tumour size, secretion and compliance with hormone replacement therapy, visual acuity and subfertility. Treatment of pituitary tumors is incomplete and the desired outcomes cannot be achieved unless all these factors have been addressed. This study would enable us to examine and rectify the causes of poor post-treatment outcomes.

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MATERIALS AND METHODS

This **r**etrospective followed by a prospective study was conducted at the Endocrine Clinic of MIDEM and JPMC, Karachi from 1st January 2012 to 31st July 2022. A non-probability purposive sampling technique was used to recruit the participants. All patients, irrespective of gender, with diagnosed pituitary tumours who had undergone medical or surgical treatment were enrolled. Those patients with incomplete medical records and patients less than 12 years of age were excluded from the study.

Informed verbal and written consent was acquired from the study participants. Already built in proforma for the study was filled for compliant and non-compliant patients. Study was started after taking the approval of the institutional review committee of the hospital. All those patients fulfilling the inclusion and exclusion criteria were included in the study. Data regarding age, gender, duration of disease, mode of treatment received was obtained and noted. Data was entered and analyzed by using SPSS-22. Pre- and post-treatment biochemical parameters among patients were tested using paired student t-test. A p-value of below 0.05 was considered as statistically significant.

RESULTS

The mean age was 36.4±10.6 years and female predominance was seen (Table 1). The type of pituitary tumours, their clinical characteristics and treatment that was offered is shown in Table 2.

The difference between mean prolactin levels prior and after the treatment (1390.048±2646.986 versus 116.360±163.369) were found to be statistically significant p<0.001). Similarly, IGF was improved post treatment indicating tumour stability. Moreover, the level of FT4 was significantly increased from 1.21±1.59 to 1.49±1.64, p<0.0001 indicating adequate thyroxine replacement (Table 3).

Table 1: Demographics and clinical parameters of study participants (n=173)

Parameter	Mean±SD, No. (%)
Age (years)	36.4±10.6
BMI (kg/m^2)	27.9±6.33
Duration of disease (years)	4.43±2.53
Gender	
Female	97 (56.1%)
Male	76 (43.9%)
Marital status	
Married	132 (76.3%)
Single	41 (23.7%)
No. of Children	
0	63 (36.4%)
1-2	49 (28.4%)
3-4	36 (20.8%)
4+	25 (14.4%)

Table 2: Clinical characteristics of the patients

Variable	No.	%
Type of Pituitary Tumour		
Prolactinoma	76	43.9
Nonsecretory	47	27.2
Acromegaly	43	24.9
Cushing's Disease	4	2.3
Craniopharyngioma	2	1.1
Gonadotropinoma	1	0.6
MRI Findings		
Macroadenoma	126	72.8
Microadenoma	47	27.2
Surgical Treatment		
Yes	74	42.8
No	74	42.8
Advised (Lost to follow up)	25	14.4
Medical Treatment		
Cabergoline	136	78.6
Octreotide LAR	29	16.8
Bromocriptine	5	3.5
Ketoconazole	2	1.2
Stereotactic Radiosurgery (SRS)		
Yes	20	11.5
No	151	87.3
Advised (Lost to follow up)	2	1.2
Conventional Radiotherapy		
Yes	36	20.8
No	137	79.2
Under Follow-up		
Yes	124	71.7
No	49	28.3

Table 3: Pre- and post-treatment biochemical parameters among patients

Variable	Pre-treatment	Post-treatment	p-value
Prolactin(n=104)	1390.048±2646.986	116.360±163.369	<0.001
IGF (n=42)	659.9±316.9	321.7±249.3	0.021
Cortisol (n=37)	13.53±18.16	10.39±5.27	0.002
FT4 (n=86)	1.21±1.59	1.49±1.64	<0.0001

Table 4: Improvement in sexual life, vision and subfertility

Parameter	No.
Effect on sexual life	
Unaffected	69
Affected	60
Improved (Post Treatment)	44
Vision	
Unaffected	53
Affected	120
Improved (Post Treatment)	85
Headache	
Yes	164
No	9
Improved (Post treatment)	138
Menstrual irregularities (females)	
Amenorrhea	37
Regular	10
Menopause	3
Irregular	3
Oligomenorrhea	4
No Data	40

Post-treatment 85(70.2%) of patients were reported improved vision. Headache was observed in 164(94.8%) of patients. In female patients, 38(39.2%) suffered from amenorrhea while for 40(41.2%) there was no data present as they were lost to follow-up (Table 4).

DISCUSSION

Comprehensive treatment of pituitary adenoma comprises of tumour control through surgery/radiation, control of excess hormone production, and lifelong replacement of deficient hormones[12,13]. In this study, patients with pituitary tumour had significant initial improvement in their clinical symptoms, and prolactin and IGF-1 levels post treatment. In addition, patients had improvement in their sexual performance, vision, and general quality of life after receiving hormone replacement post definitive therapy. However, adherence to regular follow-up was less than desirable. Factors leading to poor follow-up need to be addressed. Many patients are resident outside the city and some hail from remote areas. Women in particular need chaperones, who may not be available. There is not well-developed primary and secondary health care system, by virtue of which continuity of ongoing care cannot be provided locally. Fragmented health care system, poverty, low literacy and in particular low awareness of health and health literacy, results in our patients presenting very late with larger tumours[14]. There is also a lack of multi-disciplinary care in the outreach areas where both endocrinologists and neurosurgeons could provide continuous care[15]. Detailed written instructions for future follow-up should be given at the time of discharge, so that doctors treating them in their area of residence are fully aware of their postoperative care requirements.

Pituitary adenomas are uncommon, so there are not many published reports on the long-term outcome and prognosis of patients in our countr[16]. Our results show that microadenoma patients were less likely to develop corticotropin deficit or secondary hypothyroidism than macroadenoma patients, entirely in keeping with what is already known. Our study shows that vision was affected in (69.9%) and (70.2%) had improvement in visual function post-treatment, similarly Karki et al[17] reported that patients with large PAs had better visual recovery (78.1%), gross complete resection (84.4%), in comparison to patients with giant PAs (71.2% and 74.6%, respectively). We were unable to formally asses QOL in our patients due to retrospective nature of this analysis. This study had certain limitations. First of all it is fraught with deficiencies in data collection on account of its retrospective nature. A small sample size also limits the generalizability of the findings. Thus, further large scale prospective and multicenter studies are warranted. This study does give an overall picture of the spectrum of presentation of pituitary tumours in tertiary care centres, spanning private as well as public sector tertiary healthcare facilities in Karachi. It also highlights serious deficiencies of on-going care, thus limiting optimal treatment benefit to the patients with pituitary tumours.

CONCLUSION

The majority of patients had improvement in symptoms of pituitary tumours including sexual life, visual acuity and general quality of life. Biochemical parameters including prolactin and IGF-1

Conflict of interest: Nil

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