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Research Paper

Assessment of the Correlation between MRI Findings and Levels of Prolactin and TSH among Pituitary Adenoma Patients

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ABSTRACT:

BACKGROUND:

Pituitary adenomas are tumors of the anterior pituitary. Most pituitary tumors are slow-growing and benign. They are classified based on size or cell of origin. Pituitary adenoma can be described as microadenoma, macroadenoma, and giant tumors based on size.

OBJECTIVE:

the present study aimed to assess the correlation between MRI findings and levels of prolactin and thyrotropin in addition to other characteristics of the patients.

PATIENTS AND METHODS:

An observational correlation study design conducted at Al-Yarmouk Teaching Hospital in the Department of Radiology from 1st of January 2021 through December 2021. The current study involved 101 patients as (22 males) and (79 females) (age ranging from 15- 60 years) as an outpatient with abnormal hormonal assay on lab investigations.

RESULTS:

Patients with microadenomas and macroadenomas were significantly older than those with normal findings, the mean age was 35.6±8.7 years, 40.6±11 years and 31.2±10.6 years, respectively, (P. value <0.05). Overall pituitary adenomas (micro and macro adenomas) were more frequent in females than males compared to normal findings, (P. value <0.05). Microadenomas were significantly more frequent than macroadenomas in obese (BMI=25-35) patients, 29.2% vs. (0%), respectively.

CONCLUSION:

Neuroimaging is an essancial method for evaluation of pituitary adenoma , Pituitary microadenomas more frequent in young adult , female patients with significant correlation to elevated prolactin levels. Macroadenomas more frequent in older , obese female patients .

KEYWORDS: Pituitary adenoma, neuroimaging, serum prolactin, thyroid stimulating hormone(thyrotropin).

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Iraqi postgraduate medical journal, 2024; Vol. 23(1): 113-119
DOI: 10.52573/ipmj.2024.182812, Received: July 3, 2022, Accepted: August 15, 2022

INTRODUCTION:

The **pituitary gland** is a major gland of the endocrine system. It secretes hormones that control the actions of other endocrine organs and various tissues around the body [1].

Pituitary adenomas which were recently renamed pituitary neuroendocrine tumors (PitNET) which was proposed by the International Pituitary Pathology Club are tumors of the anterior pituitary [1]. Most pituitary tumors are slow-growing and benign. They are classified based on size or cell of origin. Pituitary adenoma can be described as microadenoma, macroadenoma, and giant tumors based on size. Microadenoma is a tumor less than 10 mm, while macroadenoma describes a tumor larger than 10 mm. Giant pituitary tumors are bigger than 40 mm. Patients with pituitary adenoma need to be evaluated by a multidisciplinary team that should include endocrinology, radiologist, and neurosurgery [1,2]. The pathogenesis of pituitary adenoma remains unknown. Genetic mutation is rarely a feature of pituitary adenoma. Familial cases of pituitary adenomas represent 5% of all pituitary tumors [3].

Magnetic resonance imaging is the imaging of choice for the pituitary gland. In order to optimize the study, it is necessary to perform thin sections (2mm or 3mm) targeted to the pituitary fossa and performed in both the sagittal and coronal planes.

T1 weighted sequences before and after intravenous contrast are the mainstay of pituitary imaging. Coronal T2 weighted sequences can also give added information but are less sensitive in the detection of adenomas [4].

Pituitary macroadenomas can extend superiorly into the suprasellar cistern and impinge on the optic nerves and/or optic chiasm to produce visual field abnormalities (typically a bitemporal hemianopia). This may be associated with symptoms or signs related to involvement of the cranial nerves that run in the cavernous sinus [5]. Pituitary microadenomas are confined within the sella and are sometimes identified within the normal pituitary gland as an area of lower signal on T1 weighted sequences than the normal pituitary tissue [6].

The aim of the present study was to assess the correlation between MRI findings and levels of prolactin and TSH in addition to other characteristics of the patients.

PATIENTS AND METHODS:

The present observational correlation study was conducted at Al-Yarmouk Teaching Hospital in the Department of Radiology from January to December 2021.

The current study involved 101 patients (22 males and 79 females) whose ages ranged between (15-60) years with abnormal hormonal assay on lab. investigation including prolactin level (> 25 ng/ml) and thyroid stimulating hormone TSH > (4.7 ng/ml) with normal T3 and T4 level or normal ultrasound assessment of thyroid gland.

All patients suspected to have pituitary adenoma based on abnormal lab tests of prolactin and TSH hormones were included in the study, while pregnant women, patients with apoplexy, Cushing disease, large or invasive pituitary tumors and para seller space occupying lesions, traumatic seller lesion, patients with previous surgery of the pituitary gland and patients with elevated both serum prolactin and TSH were excluded from this study.

The study is held with three Tesla PHILIPS MRI machine [Netherland] as a dynamic study protocol of the pituitary gland with the patient lying supine and his/her head inside the coil. An initial native study of survey -T1 WI (coronal and sagittal plains) and T2 WI axial. Then T1 WI coronal dynamic contrast study [small field of view coronal plane obtained at multiple locations through the gland component at multiple time point], and T1 delayed study in the coronal and sagittal planes were performed.

Nonionic/low Osmolality Godalinium-containing contrast Agent ((Dimeglumine gadopentetate (Magnevist) (R) as Avial of 20 ml injectable solution of 469 mg/ml) was used. The dose of gadolinium i.v contrast was 0.2 ml/kg (0.1 mmol/kg) administered as a manual bolus dose of intravenous injection.

The duration of imaging study in general was completed within ten minutes. The study was interpreted by two radiologists, and two dimension linear measurements were taken manually for visible adenomas in the post contrast delayed images. There were no real limitations during the study, and all patients tolerated well the contrast injection. The decision to perform MRI study was based on the clinical judgment of the referring (physician or neurologist).

The study was approved by the local thesis committee of the scientific council of IRAQI board of medical specialization and Radiology department at Al-Yarmouk Teaching hospital. Also verbal consent was obtained from each participant prior to data collection after explanation the aim of study.

Statistical analysis

Data were analyzed using the statistical package for social sciences version 26, and variables and study parameters were presented as mean, standard deviation, frequencies and percentages accordingly. Cross-tabulation and Chi-square test was used to assess the significance of correlation between hormonal levels and size of adenomas. Level of significance, P value of ≤ 0.05 was considered significant.

RESULTS:

A total of 101 patients were enrolled in this study. The mean age of the studied group was 34.4±10.8 (range: 15-60) years and almost two thirds (67.3%) of the patients were at the age 21-40 years. Females were dominant contributing for 78.2% with a female to male ratio of 3.6:1 as shown in table (1).

Table 1: Demographic characteristics of the studied group.

Variable		No. (%)
Age (year)	≤ 20	9 (8.9%)
	21 - 30	36 (35.6%)
	31 - 40	32 (31.7%)
	41 - 50	13 (12.9%)
	51 - 60	11 (10.9%)
Mean (SD)	34.4 (10.8)	-
Gender	Female	79 (78.2%)
	Male	22 (21.8%)
Total		101 (100%)
SD: standard deviation of mean		

According to the MRI findings, microadenomas were relatively more frequent than macroadenomas which were found in 25(24.8%) and 22(21.8%) of the patients, respectively. MRI revealed normal findings among 54 (53.5%) patients, as observed in table (2).

Table 2: Distribution of the studied group according to the size of pituitary adenomas.

Size	No. (%)
Microadenoma	25(24.8%)
Macroadenoma	22(21.8%)
Normal	54 (53.5%)

Cross-tabulation for the correlation between MRI findings and prolactin levels revealed a significant correlation between pituitary adenoma size and elevated prolactin level, where 96% of patients with microadenoma and 45.5% of those with macroadenoma had elevated prolactin level with significant correlation, (P. value = 0.001), as shown in table (3).

Table 3: Cross-tabulation for the correlation between prolactin level and MRI finding of the studied group.

MRI finding	Prolactin level		Total
	Elevated	Normal	
	No. (%)	No. (%)	No. (%)
Microadenoma	24 (96.0%)	1 (4.0%)	25 (24.8%)
Macroadenoma	10 (45.5%)	12 (54.5%)	22 (21.8%)
Normal	37 (68.5%)	17 (31.5%)	54 (53.5%)
Total	71 (70.3%)	30 (29.7%)	101 (100%)
P. value = 0.001 (significant)			

For macroadenoma, the figures were not much different, where sensitivity was 71%, specificity 92%, accuracy 83.5%, positive predictive value of 89.9% and negative predictive value of 76%. Despite the validity parameters for microademoas but did not significantly different than those for macroadenomas, (P>0.05), were relatively higher, However, the differences in validity parameters. Moreover, pooled (overall) validity for pituitary tumor; sensitivity, specificity, accuracy PPV, and NPV were 74%, 94.9%, 86.5%, 91.2% and 77.3%, respectively as observed in table (4).

Table 4: Validity parameters for the correlation between prolactin level and size of adenomas according to MRI findings.

Parameter	Microadenoma	Macroadenoma	Pooled (overall) for pituitary tumor	P. value*
Sensitivity	74.3%	71.0%	74.0%	0.940 ns
Specificity	95.2%	92.0%	94.9%	0.879 ns
Accuracy	86.8%	83.5%	86.5%	0.902 ns
PPV	93.3%	89.9%	91.2%	0.914 ns
NPV	78.7%	76.0%	77.3%	0.797 ns
Z test for proportions used in comparison ns: not significant				

Regarding correlation between TSH level and MRI findings, it was statistically insignificant, (P.value >0.05), where majority of the patients with microadenomas, macroadenomas and those with normal pituitary gland had normal TSH levels, nonetheless, higher frequency of elevated TSH level, (22.7%), reported in patients with macroadenomas compared to (16%) in those with microadenomas and 20.4% in those with normal MRI findings as illustrated in table (5).

Table 5 : Cross-tabulation for the correlation between TSH level and MRI finding of the studied group.

MRI finding	TSH level		Total
	Elevated	Normal	
	No. (%)	No. (%)	No. (%)
Microadenoma	4 (16.0%)	21 (84.0%)	25 (24.8%)
Macroadenoma	5 (22.7%)	17 (77.3%)	22 (21.8%)
Normal	11 (20.4%)	43 (79.6%)	54 (53.5%)
Total	20 (19.8%)	81 (80.2%)	101(100.0%)
P. value = 0.836 (not significant)			

Regarding TSH level, for microadenoma, elevated TSH level had sensitivity of 16%, specificity of 80%, accuracy 59%, PPV 27% and NPV of 67%. For macroadenoma, sensitivity was 23%, specificity 80%, accuracy 63%, PPV of 31% and NPV of 72%. No significant difference in validity parameters for microademoas and macroadenomas, (P>0.05). Moreover, pooled (overall) validity of TSH for pituitary tumor size revealed sensitivity, specificity, accuracy PPV, and NPV were 45%, 66%,61%, 29% and 80% respectively as shown in table (6).

Table 6 : Validity parameters for the correlation between TSH level and size of adenomas according to MRI findings.

Parameter	Microadenoma	Macroadenoma	Pooled (overall) for pituitary tumor	P. value*
Sensitivity	16%	23%	45%	0.813
Specificity	80%	80%	66%	0.714
Accuracy	59%	63%	61%	0.984
PPV	27%	31%	29%	0.983
NPV	67%	72%	80%	0.957
Z test for proportions used in comparison ns: not significant				

DISCUSSION:

Detection of pituitary adenomas varies significantly depending on the characteristics of the methods of identifying cases, the findings sought in people with symptoms associated with damage to the gland or accidental observations in diagnostic images [7,8].

Size and activity of these tumors are important factor contribute to the development of symptoms, for instance, large adenomas could compress the optic chiasm causing visual disturbances or loss, also large tumors can cause pituitary failure. Hormone producing adenomas, in addition, lead to hormone-related effect [9-11].

The present study found that the mean age of patients at the time of inclusion in the study was 34.4 ± 10.8 years, and 67.3% of the patients were young adult between 21-40 years of age. Females were dominant among the studied group and contributed for 78.2% in a female to male ratio of 3.6 to one. These findings were not unexpected and consistent with epidemiological picture of pituitary adenomas where most pituitary tumors occur in young adults and more frequent in females [12,13].

According to MRI findings, microadenomas were relatively more frequent than macroadenomas and both contributed for 46.5%, however, normal MRI findings reported in 53.5% of the patients, previous studies supported our findings in this regard [14,15].

The present study found elevated prolactin levels in majority of patients which could be attributed to the functioning prolactin secreting adenomas.

The present study found a significant association between MRI findings, microadenomas and elevated prolactin levels among the studied group, where small size adenomas significantly associated with higher levels of prolactin compared to those with normal MRI findings, (P. value = 0.001).

These findings were consistent with that reported in previous studies; earlier study conducted in 2005 by Bayrak et al. [16] from United States of America found a significant correlation between small size of pituitary adenomas and prolactin levels. Bayrak et al. also found that 11% of patients with microadenomas had prolactin level of >200 ng/ml, on contrary, 44% of patients with macroadenomas had prolactin levels between 25 and 200 ng/ml, and concluded that despite the positive correlation between small size of adenomas and prolactin levels, some macroadenomas detected in patients with only moderately elevated prolactin. Hence, Bayrak et al. suggested that pituitary MRI should be utilized in all patients with persistent elevated prolactin levels [16].

Also our findings supported by a recent study conducted in 2021 by Wright et al. [17] who documented a statistically significant direct correlation between tumor size and serum prolactin levels in functioning adenomas while no significant correlation in non-functioning adenomas. Wright and his colleagues concluded that MRI can accurately differentiate between functioning and non-functioning pituitary gland adenomas.

From other point of view, Zielinski et al. [18] documented preoperatively, the size of adenomas was significantly associated with serum prolactin levels.

The present study found no significant correlation between TSH levels and size of tumor where majority of the patients with microadenomas, macroadenomas and those with normal pituitary gland had normal TSH levels, nonetheless, higher frequency of elevated TSH, (22.7%), reported in patients with macroadenomas compared to (16%) in those with microadenomas, the non-significance could be attributed to the small number of patients with microadenomas and macroadenomas among the studied group and for more precise assessment of this correlation it is better to conduct a case-control study with larger sample size including patients with pituitary adenomas and controls, however, this is difficult to be applied because we have to perform MRI to healthy individuals.

In most patients with TSH-producing pituitary tumor diagnosis is complicated and possible misdiagnosis was not uncommon [19] previous studies documented that in 80% - 85% of TSHomas macroadenomas were reported reflected an association between higher TSH levels and larger size of adenoma.

But, microadenomas are frequently found in TSH-producing adenomas. Therefore the results regarding the correlation between TSH levels and size of tumor are still under debate and need further studies [19].

Takamizawa et al. [20] found that non-functioning pituitary adenomas showed normal levels of TSH. On the other hand, Takamizawa et al. documented that other hormonal levels were significantly associated with tumor size.

In contrast, Yamada et al. [21] found that TSH levels significantly increased with larger size of pituitary adenomas.

CONCLUSION:

The current study showed that MRI is an essential method to assess pituitary adenoma. Pituitary microadenomas were shown to be more frequent in young adults, female patients with significant correlation to elevated prolactin levels. There was a significant correlation between increased prolactin levels and pituitary microadenoma on MR imaging.

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