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ORIGINAL ARTICLE

The mean relative signal intensity ratio (SIR) difference in patients undergoing dynamic contrast enhanced magnetic resonance imaging (DCE MRI) for diagnosis of pituitary microadenoma.

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ABSTRACT… Objective: To determine the mean relative signal intensity ratio (SIR) difference in patients undergoing dynamic contrast-enhanced magnetic resonance imaging (DCE MRI) for the diagnosis of pituitary microadenoma. **Study Design:** Descriptive, Cross-sectional study. **Setting:** Radiology Department, Allied Hospital I, Faisalabad. **Period:** 5th April 2021 to 4th October 2022. **Material & Methods:** A total of 65 individuals undergoing magnetic resonance imaging with dynamic contrast enhancement of pituitary gland of any gender aged between 20 and 60 years were encompassed. Patients taking any medication (antipsychotics, anti-depressants, opiates or antiemetics), hepatic or renal failure, uncontrolled DM and hypothyroidism were excluded. Senior radiologist interpreted the DCE MR images. Pituitary microadenoma was assessed according to operational definition. For all patients, a region of interest (ROI) was defined on the area displaying varying enhancement, specifically identified as zone A. Amongst the entire patient population, a second ROI was made in the pituitary gland's normal-appearing tissue identified as zone B. Signal intensity time curves were created for all patients using both SIR T and SIR P, and the disparity between SIR T and SIR P was calculated. Relative SIR difference was calculated. **Results:** In my study, mean relative signal intensity ratio (SIR) difference in patients undergoing the utilization of DCE MRI for detecting pituitary microadenomas was 0.212 ± 0.181. The relative SIR difference on DCE MRI in patients with pituitary microadenoma was 0.35 ± 0.12 and in patients without pituitary microadenoma it was 0.03 ± 0.01. **Conclusion:** This study concluded that estimation of pre contrast T1 signal intensity ratio of a potentially abnormal lesion in dynamic contrast-enhanced MRI can enhance the accuracy of the diagnosis for locating microadenoma.

Key words: Dynamic Contrast Enhanced, Pituitary Micro Adenoma, Signal Intensity Ratio.

INTRODUCTION

Pierre Marie, a French neurologist based at Salpetriere Hospital in Paris, holds the distinction of being the first to document a condition associated with the pituitary gland. In 1886, he examined two patients displaying clinical manifestations that he labeled as acromegaly, proposing a connection between the symptoms and the involvement of the pituitary gland in the disease's development. Pituitary tumors are prevalent types of neoplasms, and it is crucial to recognize their manifestations promptly, as achieving a positive therapeutic outcome is contingent upon early detection of the lesion.

The history of pituitary tumor biology is extensive. A recent genetic analysis conducted on the dental remains of an Irish individual afflicted with gigantism, measuring 7 feet and 7 inches in height, who lived between 1761 and 1783 and was housed at the Hunterian Museum in London, unveiled the presence of a mutation in the AIP gene (c.910 C-T mutation). Strikingly, this mutation was also identified in four families with pituitary tumors from Northern Ireland. Notably, the genetic analysis indicated shared haplotypes between this historical patient and contemporary families under investigation. In 1909, Harvey Cushing and Sir Arthur Keith examined the skull

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of the index patient, confirming an enlarged pituitary fossa. Advances in genetic technology, as exemplified by Chahal et al., now enable a compelling exploration into the roots of human diseases spanning potentially over 57 generations.[1]

The existence of asymptomatic pituitary adenomas in humans has been recognized for nearly a century. Assessments of their frequency in post-mortem investigations have fluctuated, ranging from 14.7% to 37%, with an average of 10.7%, primarily identified as prolactinomas through immunohistochemistry. In magnetic resonance imaging (MRI) studies involving healthy adult volunteers, observed pituitary "hypointensities" have varied from 10% to 40%.[1] Pituitary adenomas constitute a diverse category of lesions originating from pituitary gland, with prevalence estimates ranging from 14.4% to 22.5% in the overall populace. Historically, these have been categorized according to their dimensions, with macroadenomas surpassing 1 cm and microadenomas measuring under 1 cm.[2] There are several subtypes of microadenomas that release various hormones, such as prolactin, adrenocorticotropic and growth hormones. It is critical to make the proper clinical diagnosis of the microadenoma and subtype.[3]

Early diagnosis of pituitary microadenoma is of paramount importance for treatment and prognostic purposes.[4] For the detection and localization of microadenomas, magnetic resonance imaging (MRI) has largely supplanted computed tomography (CT), which continues to be known as standard in pituitary imaging.[5] The earliest MR sequences employed for identifying pituitary adenomas were spin echo (SE) sequences, however, their effectiveness, particularly in detecting microadenomas, was limited. Subsequent research indicated that the capability to identify microadenomas improved with contrast-enhanced studies, and this effectiveness was contingent on the time lapse between contrast administration and image acquisition. The proposal for an initial dynamic scan arose as a technique to amplify the contrast distinction between the regular gland and microadenoma.[2]

The diagnostic efficacy for detecting these lesions has been significantly improved through dynamic pituitary MRI with contrast scanning, establishing itself as the standard reference.[6] Dynamic contrast enhanced MRI for pituitary imaging is conducted with a standard temporal resolution of 20–30 seconds and an in-plane spatial resolution of under 1 mm. This setup facilitates the qualitative assessment of both the pituitary gland and pituitary adenoma. In the majority of instances, there is more pronounced enhancement observed in the pituitary gland compared to a pituitary adenoma.[7] The rising false positivity in dynamic MRI is a serious issue. As of right now, no one MRI sequence has been proven to be clearly optimum for their identification, As a result, the diagnosis relies on a composite analysis of images obtained before, during, and after the administration of contrast. The relative SIR difference on DCE MRI in patients with pituitary microadenoma was 0.215 ± 0.205 and in patients without pituitary microadenoma it was 0.037 ± 0.028.[2]

Precise localization of the apparently normal pituitary gland before surgery is crucial due to the risk of hormone deficiency, a significant complication associated with transsphenoidal surgery for the removal of pituitary adenomas. As of my last available information, there is no local data on this specific aspect. This study aims to leverage signal time curve (STC) analysis by combining the advantages of the precontrast T1 SE sequence with dynamic contrast enhanced magnetic resonance imaging for assessment of microadenomas in pituitary gland. Its primary objective is to investigate whether the estimation of the precontrast T1 SIR of a tumor looking region on a DCE MRI scan can enhance the accuracy of diagnosing and locating microadenomas.

OBJECTIVES & OPERATIONAL DEFINITIONS

The objective of the study was:

- "To determine the mean relative signal intensity ratio (SIR) difference in patients undergoing dynamic contrast-enhanced magnetic resonance imaging (DCE MRI) for

diagnosis of pituitary microadenoma.
- To compare the mean relative signal intensity ratio (SIR) difference by using dynamic contrast enhanced magnetic resonance imaging (DCE MRI) with and without microadenoma."

OPERATIONAL DEFINITIONS

Pituitary Microadenoma

It was confirmed on DCE MRI when there was an intraglandular focal area showing differential enhancement (lowest signal) size between 3–10 mm in the pituitary gland after injection of contrast media. Normal pituitary gland was iso-intense on DCE MRI.

Relative signal intensity ratio (SIR) difference

It was calculated as follows:
The ratio calculated by dividing the difference in SIR by the SIR of the normal pituitary is expressed as (SIR P − SIR T)/SIR P.

Here, SIR T represents the T1 signal intensity ratio at the area of suspicion (zone a) with differential enhancement, while SIR P denotes the T1 signal intensity ratio at the normal pituitary gland (zone b).

MATERIALS & METHODS

This Descriptive, Cross-sectional study was conducted at Department of Radiology, Allied Hospital, Faisalabad from 5th April 2021 to 4th October 2022. The sample size was calculated By using WHO sample size calculator Population mean = 0.215[2]

Population standard deviation = 0.205[2] Absolute precision required (d) = 0.05 Confidence level = 95%. The Sample size was 65 and the sample technique employed was Non-probability, consecutive sampling.

SAMPLE SELECTION

Inclusion Criteria

a. Patients age ranges from 20-60 years of both genders.
c. Patients undergoing magnetic resonance imaging of the pituitary gland with dynamic contrast enhancement.

Exclusion Criteria

a. Patients taking any medication (antipsychotics, anti-depressants, opiates or antiemetics) that affect the functions of pituitary gland.
b. Patients having hepatic or renal failure.
c. Patients with uncontrolled diabetes mellitus (HbA1c > 7).
d. Patients with hypothyroidism.

Data Collection Procedure

Following approval from the hospital's ethical committee, patients meeting the inclusion criteria were recruited, and informed consent was obtained. To evaluate the morphology of the pituitary and brain, a pre-contrast coronal VIBE sequence was acquired with the following parameters: TR/TE of 497/10 ms, a matrix of 320 x 320, a field-of-view (FOV) of 230 mm, and a slice thickness of 2.5 mm without a gap. Subsequently, a coronal dynamic contrast scan was conducted using a fast SE sequence with a 15 mm FOV, 3 mm slice thickness, and a 0.2 mm slice gap after the pre-contrast sequence. Contrast (IV gadolinium) was administered at the transition between the first and second dynamics. The dynamic sequence, lasting 225 seconds, comprised a total of six cycles during and after the contrast injection, along with one dynamic from the pre-contrast study.

A senior radiologist interpreted the dynamic contrast-enhanced magnetic resonance (DCE MR) images, evaluating pituitary microadenomas based on a specified operational definition. In the region of differential enhancement (zone a) for all patients, a region of interest (ROI) was delineated. Additionally, a second ROI was established in the normal-appearing tissue of the pituitary gland (zone b) for all patients. Signal intensity time curves were generated for all patients at both SIR T and SIR P. The difference between SIR T and SIR P was computed, and the relative SIR difference was calculated in accordance with the operational definition. All data were collected using a specially designed proforma provided by the researcher.

Data Analysis Procedure

The data was input and subjected to analysis

using SPSS version 22. Descriptive statistics, encompassing mean and standard deviation, were computed for numerical variables such as age, SIR T, SIR P, SIR difference, and relative SIR difference. Frequency and percentage calculations were performed for qualitative variables like gender and the presence of pituitary microadenoma. An independent sample t-test was utilized to compare the relative SIR difference between individuals with and without microadenoma.

Variables that could influence the outcome, such as age and gender, were managed by stratification. Subsequently, an independent sample t-test was conducted post-stratification. Significance was determined by a p-value of ≤ 0.05.

RESULTS

Age range in this study was from 20-60 years with mean age of 41.74 ± 9.22 y. Majority of the patients 36 (55.38%) were between 41 to 60 years of age as shown in Table-I.

Out of these 65 patients, 42 (64.62%) were male and 23 (35.38%) were females with ratio of 1.8:1 (Figure-1). Distribution of patients according to pituitary microadenoma is shown in Table-II.

In my study, mean relative signal intensity ratio (SIR) difference in patients undergoing DCE MRI for diagnosing pituitary microadenoma was 0.212 ± 0.181 (Table-III). The relative SIR difference on DCE MRI in patients with pituitary microadenoma was 0.35 ± 0.12 and in patients without pituitary microadenoma it was 0.03 ± 0.01 (Table-IV).

Stratification of mean relative signal intensity ratio (SIR) difference in patients with pituitary microadenoma with respect to age and gender is shown in Table-V & VI respectively.

Age (years)	No. of Patients (%)
20-40	29 (44.62%)
41-60	36 (55.38%)
Total	65 (100.0%)

Table-I. Distribution of patients according to age. Mean ± SD = 41.74 ± 9.22 years

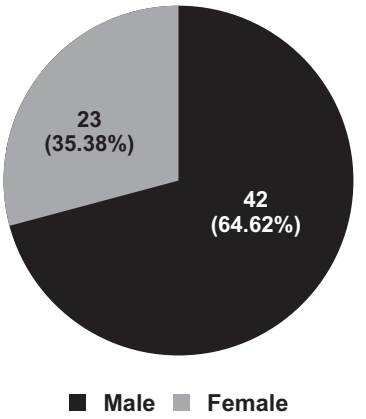

Figure-1. Distribution of patients according to gender (n=65).

Pituitary Microadenoma	No. of Patients (%)
Yes	37 (56.92%)
No	28 (43.08%)
Total	65 (100.0%)

Table-II. Distribution of patients according to pituitary microadenoma.

	Mean	SD
Relative SIR difference on DCE MRI	0.212	0.181

Table-III. Mean relative signal intensity ratio (SIR) difference in patients undergoing dynamic contrast enhanced magnetic resonance imaging (DCE MRI) for diagnosis of pituitary microadenoma.

Pituitary Microadenoma	Relative Signal Intensity Ratio (SIR) Difference		P-Value
	Mean	SD	
Yes	0.35	0.12	0.0001
No	0.03	0.01	

Table-IV. Comparison of the mean relative signal intensity ratio (SIR) difference by using DCE MRI with and without microadenoma

Age (Years)	Relative Signal Intensity Ratio (SIR) Difference		P-Value
	Mean	SD	
20-40	0.22	0.19	0.705
41-60	0.21	0.17	

Table-V. Stratification of mean relative signal intensity ratio (SIR) difference in patients with pituitary microadenoma with respect to age.

Gender	Relative Signal Intensity Ratio (SIR) Difference		P-Value
	Mean	SD	
Male	0.22	0.19	0.612
Female	0.20	0.17	

Table-VI. Stratification of mean relative signal intensity ratio (SIR) difference in patients with pituitary microadenoma with respect to gender.

DISCUSSION

Dynamic contrast enhanced MRI is a robust method offering a quantitative assessment of vessel permeability and interstitial volumes. Specifically in the brain, it delineates the permeability of the blood-brain barrier (BBB), proving to be beneficial in various applications.[8] These applications encompass the evaluation of conditions exhibiting significant blood-brain barrier breakdown, such as the gradation of brain tumors[9,10], lesions associated with multiple sclerosis[11,12], and conditions characterized by gradual and prolonged blood-brain barrier breakdown, such as diabetes[13], and Alzheimer's disease.[14] Beyond neurological applications, DCE-MRI finds utility in evaluating cancer and monitoring therapeutic interventions in various anatomical regions, including the breast[15,16], prostate[17], and hepatic.[18] DCE-MRI encounters a complex balance between attainable spatial resolution, temporal resolution, and volume coverage. Strategies for acceleration that capitalize on redundancies in the temporal dimension have demonstrated considerable promise in enhancing these trade-offs. These encompass initial methods, such as view-sharing[19-21], advanced techniques like highly constrained back projection (HYPR) and, more recently, compressed sensing.[23-28]

I undertook this study to ascertain the mean relative signal intensity ratio (SIR) difference in patients undergoing DCE MRI in diagnosing pituitary microadenomas and to compare the average relative signal intensity ratio (SIR) difference in DCE MRI between cases with and without microadenomas. In my study, mean relative signal intensity ratio (SIR) difference in individuals undergoing DCE MRI for the diagnosis of pituitary microadenomas was 0.212 ± 0.181 (Table-III). The relative SIR difference on DCE MRI in patients with pituitary microadenoma was 0.35 ± 0.12 and in patients without pituitary microadenoma it was 0.03 ± 0.01. The relative SIR difference on DCE MRI in patients with pituitary microadenoma was 0.215±0.205 and in patients without pituitary microadenoma it was 0.037±0.028.[2]

Ma et al.[29] illustrated the effectiveness of assessing relative signal intensity (tumor to white matter of frontal lobe) on pre-contrast T1-weighted images in predicting the composition of pituitary adenomas.

Nevertheless, contradictory results exist, as certain studies have suggested a lack of association between tumor consistency and signal intensity on T1-weighted MRI.[30,31] Additionally, another investigation noted a reverse relationship between signal intensity on T2W MRI and amount of collagen present, that were found to be plenty in solid pituitary adenomas.[32] Nevertheless, numerous data has not demonstrated a correlation of this nature.[30,31] A particular study indicated that reduced ADC (apparent diffusion coefficient) values correlate with a soft tissue mass density during surgery and higher cellularity in pathology.[30] On the contrary, there is a report suggesting that lower ADC (apparent diffusion coefficient) values have association with firmer tumor consistency and greater amount of collagen present.[31]

Limited research has sought to evaluate signal time curves (STCs) on dynamic contrast-enhanced MRI to gauge the pattern of enhancement over a specific period for both tumor and normal pituitary gland, aiming for increased certainty in the diagnostic evaluation. In research conducted by Yuh et al., It was discovered that adenomas affecting the pituitary gland exhibited enhancement approximately 9.3 ± 1.5 seconds after the enhancement of the straight sinus, and notably earlier (12.0 seconds) than the enhancement of the anterior pituitary.[33]

In order to determine the ideal acquisition time for microadenoma detection, Rossi Espagnet et al. investigated signal time curves (STCs) of the pituitary in a cohort of 52 patients for very first time. They came to the conclusion that 120 s is the best period for imaging.[34] Additionally, they discovered that the peak enhancement between a microadenoma and a healthy anterior pituitary exhibited notable differences. Anterior

pituitary gland demonstrated an earlier peak enhancement, with a mean time-to-peak of 80 seconds, while the pituitary microadenoma exhibited a mean time-to-peak of 90 seconds.

According to a study conducted by Stadnik et al. involving 12 patients with microadenomas, both the pre-contrast T1 sequence and dynamic contrast-enhanced MRI (DCE MRI) were effective in detecting 84% (10 out of 12) of the lesions. However, the combination of dynamic MRI with the pre-contrast T1 sequence achieved a 100% detection rate for all cases.[35] In their study, Ma et al. noted a substantial correlation between the signal intensity on pre-contrast T1 SE sequences and the consistency of tumors, specifically in relation to the expression of collagen IV.[36]

It is commonly recognized that the pituitary gland exhibits a more pronounced contrast enhancement compared to the macroadenoma.[37-39] This characteristic is probably attributed to disparities in the vasculature between the normal pituitary tissue and adenomatous tissue.

Several earlier investigations have histologically indicated that the vascularization of a pituitary adenoma is comparatively weaker than that of a normal pituitary gland.[40,41] Recent studies employing objective mathematical models have suggested that the vascular supply to the normal pituitary gland is characterized by a more intricate and well-organized microvascular network compared to that of a pituitary adenoma.[42,43]

To our knowledge, there is only one previous study that endeavored to identify the pituitary gland in individuals with macroadenomas using dynamic MR imaging.[44] This research team successfully identified the pituitary gland in 28 out of 33 cases using multidetector-row CT imaging and dynamic MR imaging. However, it's important to note that their identification was solely based on subjective visualization of the preoperative scan, lacking quantitative confirmation. Moreover, the authors did not provide information on the mean size of the macroadenomas in their patient population, which is a significant factor as localizing the normal pituitary gland becomes challenging in larger macroadenomas. Therefore, the use of submillimeter voxel thickness is crucial when acquiring data. In the mentioned study, dynamic studies were conducted with 3-mm-thick sections

CONCLUSION

The results of this study suggested that the mean relative signal intensity ratio (SIR) difference, observed in individuals undergoing dynamic contrast enhanced magnetic resonance imaging (DCE MRI) for the diagnosis of pituitary microadenoma was 0.212 ± 0.181. This value is notably elevated compared to the normal pituitary gland. Therefore, it is recommended that DCE MRI be routinely conducted for the diagnosis of pituitary microadenoma, specifically to estimate the precontrast T1 signal intensity ratio (SIR) of suspicious lesions. This approach is advised to enhance the diagnostic accuracy in localizing microadenomas.

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