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Diagnostic Accuracy of Non-Contrast Magnetic Resonance Imaging in Diagnosing Pituitary Micro-Adenoma, Taking Histopathology as Gold Standard

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ABSTRACT

Background: Pituitary microadenomas (PMs) are common benign tumors that are often not visualized even when they are present due to their asymptomatic nature. The objective of the study was to evaluate the diagnostic accuracy of non-contrast magnetic resonance imaging (MRI) in the diagnosis of pituitary microadenomas using histopathology as a gold standard.

Methods: This cross-sectional validation study (IRB Approval No. IRB/18/2024/01) included 121 patients presenting with severe headaches and focal brain lesions on CT scans at Doctors Hospital, Lahore from September 2024 to November 2024. In this cross-sectional study, a non-probability consecutive sampling technique was used. A standardized protocol was used for non-contrast MRI and findings were interpreted by experienced radiologists. The comparison was made against histopathology as the reference standard. A 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value and negative predictive value, and overall diagnostic accuracy by using SPSS version 25.

Results: Of 121 patients (mean age 40.74 ± 10.35 years), 70 (57.9%) were females. Non-contrast MRI showed a sensitivity and specificity of 37.25% (38/102) and 89.47% (17/19) respectively. Specificity is high, meaning that the modality is reliable in eliminating false positives, but sensitivity is low, which means that it won't find true positives correctly. The percentage of diagnostic accuracy was 45.5% (55/121) which showed that the technique had room for significant improvement.

Conclusion: Pituitary microadenomas can be clinicopathologically screened using non-contrast MRI as an initial radiation-free diagnostic modality with minimal ionizing and contrast agents-based risk being valuable for long-term monitoring.

Keywords: Pituitary Microadenoma, Non-Contrast MRI, Histopathology, Endocrine Tumors.

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INTRODUCTION

Pituitary adenomas (PA) are noncancerous tumors with a prevalence of 1 in 865 to 1 in 2,688 adults. These tumors can secrete excess hormones or exert pressure on surrounding structures resulting in varied clinical manifestations such as infertility, diabetes insipidus, and hypopituitarism[1]. Pituitary tumor, while benign, can prevent the normal production of follicle-stimulating hormone (FSH) or luteinizing hormone (LH), leading to infertility. Patients with infertility are often diagnosed with hormone-secreting PAs, such as prolactinomas. Pituitary adenomas are 50% microadenomas, including 90% prolactinomas, and rarely extend beyond the sellar[2]. Since pituitary microadenomas (PMs) were noted to be asymptomatic to a large extent, their timely diagnosis and follow-up with particular emphasis on functional PMs could be essential to avoid complications and could provide adequate therapeutic strategies, in case necessary, including medical, surgical, or radiological management[3]. Moreover, early detection was reported to help target hormonal treatments that could help improve fertility outcomes and lower long-term risk of endocrine dysfunctions. Proper monitoring was suggested to detect tumor growth or transformation requiring more aggressive treatment strategies[4].

The development of no contrast MRI based on diffusion-weighted imaging and other T2 sequences may provide a better characterization of the lesion and may allow distinguishing between different types of tumors. They could make several clinical radiography SOPs less time-consuming and also increase the availability of imaging for patients that cannot undergo contrast-enhanced imaging [5]. Rathke's cysts, mostly occurring in the midline, and off-midline cysts (cystic microadenomas) could be included under those. Since these lesions could approach the resolution limit of MRI scanners, the diagnostic overlap was noted to be high. MRI of the pituitary was performed using both sagittal and coronal planes with thin sections (2–3 mm) and a small field of view focused on the pituitary gland[6]. Evaluation of solid microadenomas revealed them as areas of delayed contrast enhancement using T1-weighted imaging performed before and after administering gadolinium contrast. Nevertheless, pituitary adenomas could also be detected on T1- and T2-weighted coronal and sagittal images without contrast. It could reduce examination time and costs and could avoid possible adverse consequences from contrast agents, including nephrogenic systemic fibrosis (NSF)[7,8]. Non-contrast MRI outcomes can be effectively evaluated using a contingency table, which categorizes true positives, false positives, true negatives, and false negatives against the histopathological gold standard. Therefore, non-contrast MRI up to date is considered potentially a valuable alternative for patients who require repetitive imaging or who have contraindications to contrast agents[9,10]. The objective of this study was to determine the diagnostic precision of non-contrast magnetic resonance imaging in detecting pituitary microadenoma, taking the histopathology technique as the gold standard.

METHODS

This cross-sectional validation study was conducted in the Department of Radiology at Doctors Hospital, Lahore, following approval from the Institutional Review Board (IRB Approval No. IRB/18/2024/01). After study approval, the cross-sectional study duration was 02 months (October 2024 and November 2024), with a sample size of 121 study cases calculated at a confidence level (95%) by using OpenEpi software version 3.01. The data from the age (years) of study cases was normalized using SPSS version 25, and the confidence interval (95%) was calculated based on the mean and standard error of the normalized values. A non-probability, consecutive sampling technique was employed for participant selection.

The inclusion criteria consisted of patients with severe headaches and focal brain lesions on CT scan and who planned to undergo a biopsy for histopathology, the duration of symptoms >3 months, and adult patients i.e. age range from 20-60 years of either gender. The exclusion criteria consisted of patients with a history of radiotherapy, those with repeated pituitary surgery, and those with contraindications for MR imaging (stents, claustrophobia, metallic prosthesis, pacemakers).
Informed written consent from each patient was taken. Age, gender, duration of symptoms and size of lesion were noted. Then in all patients, non-contrast pituitary MR imaging was done. Coronal and sagittal Turbo Spin Echo TSE T1 weighted multipoint Dixon (mDixon) sequences of

the sellar region, including sagittal T2 weighted thin section images, and axial T2WI or FLAIR of the brain was taken as the imaging protocol. Coronal T2WI thin section images were added or substituted for sagittal T2WI to evaluate the optic nerves, olfactory structures and hypothalamus, according to institutional protocols. Given the need for rapid exam, institutional preferences also determined the choice of imaging techniques such as the section thickness and whether 2D or 3D acquisition could be used.

Collected data was analyzed using SPSS software version 25.0. Data normality was assessed by the Shapiro-Wilk test. For continuous variables such as age, symptom duration and lesion size, descriptive statistics was calculated including mean and SD or median with IQR. For categorical variables, gender, whether or not pituitary microadenoma would be present in non-contrast MRI and histopathology, frequencies and percentages were determined. With histopathology as the gold standard, a 2×2 contingency table was constructed to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of non-contrast MRI in diagnosing pituitary microadenomas.

RESULTS

The study utilized 121 patients who have symptoms of severe headache and focal brain lesion under CT scan. The symptoms on each patient persisted not older than 3 months. The age range of patients lied from 20 to 60 years old, both male and female. The majority of the patients were 70 females (57.9%) and 51 males (42.1%). The mean age of patients was 40.74 ± 10.35 years. The statistical data of patients can be seen in (Table 1).

Table 1: Study Characteristics

Patients Characteristic N=121	Values
Age (Mean ± SD)	40.74 ± 10.35 Years
Male	39.8 ± 10.5 Years
Female	41.5 ± 10.5 Years
Frequency (Percentage)	
Male	51 (42.1%)
Female	70 (57.9%)
Duration of Symptoms	
Male	>3 months
Female	>3 months

The results showed the PPV and NPV values of pituitary micro adenoma as 95.0% (38/40) and 20.9% (17/81) respectively and calculated accuracy of 45.5% (55/121). Sensitivity and specificity of non-contrast MRI in diagnosing pituitary microadenoma as 37.25% (38/102) and 89.47.0% (17/19) respectively. The contingency table is shown in (Table 2).

Table 2: Contingency

Pituitary Microadenoma on MRI		Pituitary Microadenoma on Histopathology		
		Present	Absent	Total
	Present	38 (37.25%)	2 (10.5%)	40
	Absent	64 (62.74%)	17 (89.47%)	81
	Total	102	19	121

The microadenomas were histopathological confirmed in all patients, and hormone-secreting characteristics were expected for each condition, as expected for each condition. The following data is shown in (Table 3).

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Table 3: Distribution and Characteristics of Focal Pituitary Lesions Across Clinical Groups

Patient Frequency with %	Clinical Condition	Focal Lesion Location	Size (mm)	Imaging Findings (MR/CT)	Histopathology/Surgical Notes
41 (33.88%)	Cushing's Syndrome	Mid/Right/Left Lobe	2-7	Asymmetry, stalk deviation, probable focal lesions	2-7 mm adenomas, typical of ACTH-secreting lesions
39 (32.23%)	Hyperprolactinemia	Left/Right Lobe	3-6	Lesions mostly confined to pituitary, no extrasellar extension	3-6 mm adenomas, often prolactin-secreting
20 (16.53%)	Acromegaly	Right cavernous sinus	5-10	Some lateral extension, no extrasellar invasion	5-10 mm GH-secreting adenomas, localized effects
21 (17.36%)	Other (e.g., non-functioning adenomas, gonadotropinomas etc)	Various locations (central, lateral, extrasellar)	3-8	Heterogeneous findings; some with bony erosion, others without	3-8 mm adenomas, varying levels of hormone secretion

The results showed that non-contrast MRI showed an overall sensitivity of 37.25% to detect microadenomas with respect to histopathology and therefore indicated moderate diagnosis of true positive cases. With an overall diagnostic accuracy of 45.5%, the moderate effectiveness of non-contrast MRI in identifying microadenomas in terms of comparing histopathology, attested to the role of non-contrast MRI as a supportive, not definitive, diagnostic tool. A structured approach to the management of microadenomas was used given tumor progression or symptoms. This approach made sure that the intervention is timely thus avoiding unnecessary procedures. The flowchart of the follow-up procedure is shown in **Figure 1.**

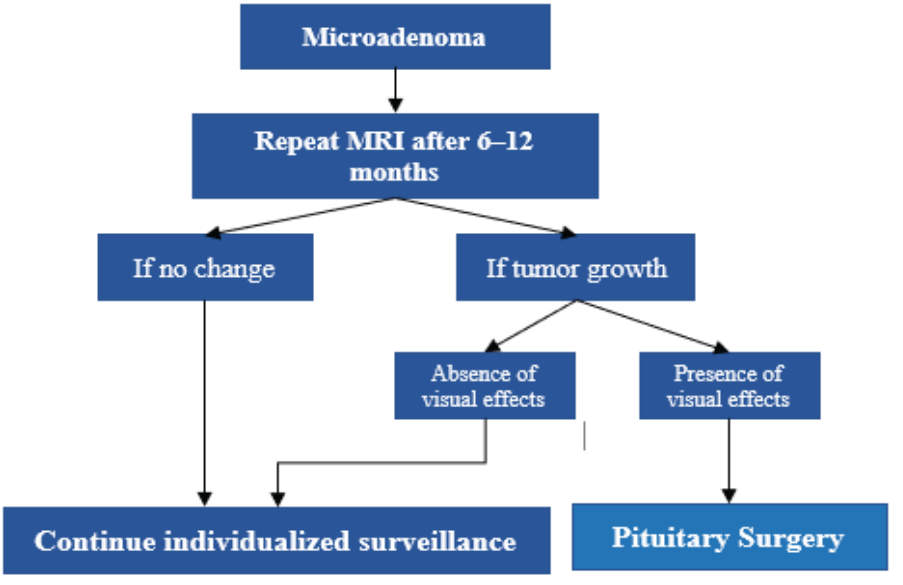

Figure 1: Follow-Up Procedure

DISCUSSION

This study showed that non-contrast imaging demonstrated moderate sensitivity (37.25%), but high specificity (89.47%), suggesting although non-contrast MRI was good at ruling false positives, it could be improved at detecting true positives[11]. The PPV was 95.5% that showed that non-contrast MRI could be reliable when it came to finding the positive predictive values. The overall 45.5% diagnostic accuracy suggested great room for improvement[12]. In particular, these findings demonstrated pros and cons of non-contrast MRI in diagnosing PM cases and the need for adjunctive diagnostic strategies.

Results of this study were consistent with other studies highlighting the usefulness and limitations of MRI for detection of PM. For example, one study described the efficacy of non-contrast MRI for pediatric pituitary endocrinopathies, in particular for its safety that was introduced by gadolinium-based contrast agents. According to this study non-contrast MRI could be used to detect specific types of pituitary tumors reliably without the need to expose patients to unnecessary interventions. Similarly, another study demonstrated the ability of thin section imaging to improve visualization of PM revealed in patients with Cushing disease where identification of tumor was notoriously problematic[13].

Yet, one study suggested that dynamic contrast enhanced MRI provided superior sensitivity in the detection of PM as compared with other imaging modalities, including CT and ultrasound (US)[14]. The results of this study were consistent with the observations of another study that highlighted MRI's limitations for differentiating PM from other cystic lesions where contrast enhancement was not available. Studies have highlighted its utility in identifying pituitary microadenomas in patients with endocrinopathies, emphasizing its safety and cost-effectiveness when compared to gadolinium-enhanced imaging. However, their study stressed that non-contrast MRI frequently underestimated tumor prevalence, especially in cases in which the adenoma was not clearly demarcated on radiological grounds [15,16]. It has been demonstrated the role of non-contrast MRI in differentiating microadenomas from other parasellar abnormalities, noting similar challenges in sensitivity but robust specificity[17]. Despite promise, advanced imaging modalities (e.g. high resolution 3T MRI) had not yet improved PM detection. Although one study pointed out that 3T MRI provided the increased spatial resolution and signal intensity to give much higher sensitivity than currently available 1.5T systems[18].

This study suggested that non-contrast MRI missed significant number of cases, resulting in potential under diagnosis due to its low sensitivity[19,20]. That underscored the need for histopathological confirmation of suspected cases, especially in patients with clinical features directing towards pituitary dysfunction[21]. On the other hand, high specificity reduced the probability of false positives, optimizing resource utilization. It is particularly important when no or little access to advanced imaging technology is available or when contrast dyes are not suitable to use in clinical settings[22,23].

Alternatively, non-contrast MRI have several advantages as well. It is cheap, safe, easy to perform and therefore should be included in the first line of diagnostic tool[24]. Moreover, the accuracy of diagnosis could be improved with integration of newer imaging techniques including MR spectroscopy or diffusion weighted imaging. These approaches offer additional metabolic and structural information from which the differential diagnosis between PM versus other sellar and parasellar lesions can be made[25].

This study had small sample size, and although the study findings were valuable, they could not be generalized to larger, more diverse populations. Data from only one centre admitted to potential biases stemming from institutional imaging practices and patient demographics. These findings should be validated in future multicentre collaborations with larger cohorts to explore non-contrast MRI's diagnostic performance. With dynamic imaging techniques, higher field MRI systems and artificial intelligence-based post processing tools, it is possible to address the gap in sensitivity observed and to increase diagnostic yield.

CONCLUSION

This study emphasized on the viability of non-contrast MRI as a safe and cost-effective imaging modality for pituitary microadenomas in resource limit settings or for patients who could not tolerate contrast agents. Its high specificity was a plus point, but it had limited sensitivity that highlighted the need for confirming the results histopathologically and use of complementary diagnostic techniques. The future work should concentrate on finding the more optimized imaging protocols and integration of the technological advancements for the benefit of the patient and overall benefit of the diagnostic outcome.

LIST OF ABBREVIATIONS

PA-Pituitary Adenoma
PM-Pituitary Microadenoma
MRI-Magnetic Resonance Imaging
FSH-Follicle-Stimulating Hormone
LH-Luteinizing Hormone
CT-Computed Tomography
NSF-Nephrogenic Systemic Fibrosis

PPV-Positive Predictive Value
NPV-Negative Predictive Value
IQR-Interquartile Range
DWI- Diffusion-Weighted Imaging
FLAIR-Fluid-Attenuated Inversion Recovery

CONFLICT OF INTEREST
There is no conflict of interest.

ETHICAL APPROVAL
This cross-sectional validation study was conducted in the Department of Radiology at Doctors Hospital, Lahore, following approval from the Institutional Review Board (IRB Approval No. IRB/18/2024/01).

AUTHOR'S CONTRIBUTION
SS, TA: conceived the idea and designed the research work, **PS, ZK:** did data analysis, **WA, GR:** did the manuscript writing, **EUH:** did proof read and editing, and All authors agreed to be accountable for all aspects of research.

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