Research Article

# The Diagnostic Accuracy of Dynamic Contrast Magnetic Resonance Imaging (MRI) in Symptomatic Patients with Pituitary Macroadenomas Taking Histopathology as Gold Standard

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**Abstract:**

**Background:** The pituitary gland also known as the "master gland," is involved in maintaining the homeostasis of various body functions. The pituitary gland is comprised of adenohypophysis and neurohypophysis, and stays in an indent in the sphenoid bone called sella turcica.

**Objective:** To determine the diagnostic accuracy of dynamic contrast Magnetic Resonance Imaging (MRI) in symptomatic patients with pituitary macroadenoma keeping histopathology as gold standard.

**Methods:** Cross-sectional study carried out in Department of Radiology, Tertiary Care Hospital, Lahore from May 2019 to Oct 2020. Prospective. One hundred and one patients (101) were enrolled. Dynamic contrast magnetic resonance imaging (MRI) of patients was performed on 1.5 Tesla GE MRI machine using head coil. Transsphenoidal endoscopic surgery of seventy-five patients was done due to their progressing symptoms and out of these four patients lost to follow up. All the available post operative specimens were reviewed by experienced histopathologist and were labelled as positive and negative for pituitary macroadenoma.

**Results:** Mean age of patients (n=71) was 37.4 years. Out of 71 patients, MRI showed pituitary macroadenoma in 64 patients (90.1%) of which two were false positives. 3 patients (4.2%) showed pituitary microadenoma, 1 ( 1.4%) represented meningioma,1 ( 1.4%) showed craniopharyngioma and 2 ( 2.8%) showed pituitary hyperplasia. Sensitivity was found to be 96.9% , specificity was 71.4% , positive predictive value (PPV) was 96.9% , negative predictive value (NPV) was 71.4% and accuracy of dynamic contrast MRI in detecting pituitary macroadenoma was 94.3%.

**Conclusion:** Dynamic contrast MRI is an authentic and non-invasive diagnostic imaging modality due to its better soft tissue contrast, multiplanar images and no risk of ionizing irradiation that allows the detection of pituitary macroadenoma with high sensitivity, specificity and accuracy. It also provides practical information about the interrelation of the gland with adjoining anatomical structures and helps to schedule medical or surgical treatment.

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**Key words:** Dynamic contrast Magnetic Resonance Imaging (MRI), pituitary, macroadenoma, diagnostic accuracy.

## Introduction:

The pituitary gland also known as the "master gland," is involved in maintaining the homeostasis of various body functions. The pituitary gland is comprised of adenohypophysis and neurohypophysis, and stays in an indent in the sphenoid bone called sella

turcica. It is attached through the infundibulum to hypothalamus, which makes ventral part of floor of third ventricle[1,2].It is encircled by cranial nerves and major blood vessels. Pituitary macroadenomas are explained as tumors arising from the pituitary with maximal diameter equal or greater than 10 mm. Prevalence of pituitary tumors is up to 15-20 % of all intracranial masses and pituitary adenomas make up approximately 90% of sellar and parasellar masses. It is the third most common tumor after meningioma and glioma in the current generation and is an important source of mortality in developing countries[3,4,5]. These tumors can be non functional or functional presenting with non specific symptoms such as headache, menstrual irregularities, galactorrhea and visual disturbances. Macro-adenomas probably produce stalk effect, in which a mild to moderate increase of prolactin hormone result from stalk compression caused by the growing tumor[6]. Pituitary masses are in close propinquity to optic chiasma, so most patients present with bitemporal hemianopia. Moreover, these tumors can also cause mass effect, so patients present with signs and symptoms of increased intracranial pressure or malfunctioning endocrine system. If not treated, approximately 50% of macroadenomas will show increasing size with more than 66% of the patients experiencing visual abnormalities.

Computed tomography (CT) has lower soft tissue resolution than MR and thus it plays a minor role in diagnosis of pituitary gland masses, but it remains useful in picking out the calcification, destruction of bones, and relevant adjacent anatomical structures keeping surgery in option. Notably, MRI is the preferred investigation in the neuroradiological field because it has excellent soft tissue contrast and it allows a precise evaluation of intracranial structures[2]. Diagnostic tests include hormonal levels, Dynamic MRI pituitary protocol with contrast and eye evaluation with fundoscopy are suggested before surgery[7].As it is important to preserve the gland as well, so preoperative imaging will help surgeons in localization. Localizing the pituitary gland becomes important for a surgeon to minimize hormonal deficiency postoperatively. Although Dynamic MRI with contrast is the standard investigation for assessment of pituitary adenomas, its role in its preoperative localization has not been completely surveyed[8]. Dynamic contrast MR has increased their detection rate and help us provide the extent, operability and surgical approach. Whether optic chiasm, internal carotid artery, cavernous sinus and cranial nerves are involved, or tumor is causing mass effect can only be found out by MRI[9].

Rationale of study is that the use of MRI may improve the quality of care for people with pituitary macroadenomas through increasing early detection of patient problem with daily functioning and well being, guiding the therapeutic management by proper diagnosis and leading to improvements in patient's health related quality of life and satisfaction with care. Although much work has been done on dynamic contrast MRI in diagnosis of pituitary macroadenoma in developed countries, its accuracy has not been evaluated much in our part of the world. This study was organized to bridge this expertise gap and to highlight importance of MRI in detecting pituitary macroadenoma and consequently in planning patient management.

## Methods:

An institutional review board approved cross sectional study was performed in Radiology Department, Tertiary Care Hospital, Lahore from May, 2019 to Oct, 2020. One hundred and one (101) patients with clinical presentation of pituitary lesion of any age and gender referred from Department of Neurology, Medicine, Ophthalmology and Endocrinology were included in the study. Sample size (n=101) was calculated by taking sensitivity 99%, specificity 29%, absolute precision 10%, expected prevalence 20% and confidence level of 95%[18]. In these cases, histological assessment of the lesion by transsphenoidal endoscopic surgery, also known as endoscopic pituitary surgery, was scheduled. Patients in whom MRI examination was considered unsatisfactory or incomplete because of motion artifact or susceptibility artifact, or subjects with recurrent disease or impaired renal function test, patients with pacemakers, prosthetic valves, aneurysm clips, plates, any other ferromagnetic material and claustrophobics were not taken into consideration.

Of all patients meeting the inclusion criteria, MR imaging at 1.5 Tesla GE MRI machine using head coil was performed. Study included pre contrast T2-

weighted imaging (TR/TE 4000/31 msec, acquisition matrix 190 x 200, small field of view (FOV) 16 x 16 cm; slice thickness 4 mm) and T1-weighted fast spin echo sequence (TR/TE 540/7 msec, acquisition matrix 190 x 200, FOV 16 x 16 cm, slice thickness 4 mm) were acquired in sagittal and coronal planes. After intravenous gadolinium contrast was administered, six to nine consecutive images were taken in sagittal and coronal plane at every 7 seconds after start of injection. In dynamic MRI routine post contrast images and delayed scan after 10 minutes were added in one study for ideal imaging. Approximately forty to fifty seconds after contrast injection, there was homogenous enhancement of the gland. Gadolinium contrast was administered at 0.2ml per kilogram of body weight for diagnosing adenomas, as they mostly show less enhancement than the normal pituitary tissue and it is important to note that the best time to view this differential enhancement is the first arterial phase of the contrast injection. Reconstructed images were sent to the PACS for reporting. The pituitary MRI scans were interpreted by experienced radiologist with more than 5 years of post-fellowship experience. The study was considered positive if the pituitary gland was enlarged or showed a sellar mass appearing hypointense on T1 weighted images, hyperintense/ heterogeneous on T2 weighted images and homogenous/ heterogeneous enhancement on contrast enhanced images[10].Patients were then sent for transsphenoidal endoscopic surgery where they were assessed for surgery and available specimens were sent for histopathological analysis. As elective surgery was suspended due to COVID-19 pandemic, surgery of some patients was also performed outside our hospital, as it is a 2500 bedded hospital which accommodates patients from all over the province. Finally, patients returned to our hospital's Radiology Department for follow up. All the specimens were reported by experienced histopathologist with 5 years of post-fellowship experience and results were obtained.

Data were entered and analyzed by using SPSS version 20 and above. Age was presented as mean. Contingency table was generated to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of MRI taking histopathology as gold standard. Data was stratified for age and gender to overcome confounding. In this study we used uniform sources of information and efficient questionnaire to avoid bias. MRI machine was standardized and checked for artifacts.

## Results:

During our study, 101 patients were enrolled. Out of these patients, surgery was only performed in 75 patients due to their progressing symptoms and visual disturbance. Four patients were lost to follow up leaving behind 71 patients. of these, 40 were women (56.3%) and 31 were men (43.7%). Mean age of study patients (n=71) was 37.4 years. Only sixty-two (87.3%) macro-adenomas were solid, six (8.5%) predominantly solid and three were (4.2%) predominantly cystic. Eight masses (11.3%) contained hemorrhage. Sixty (84.5%) were isointense, seven (9.9%) were hyperintense and four (5.6%) were heterogeneous on T1WI. Eleven (15.5%) were isointense, fifty-one (71.8%)were hyper-intense and nine (12.7%) were heterogeneous on T2WI. Twenty-five masses (35.2%) showed intense post contrast enhancement, seven (9.9%) showed peripheral post contrast enhancement, thirty-four (47.9%) showed heterogeneous enhancement and five (7.0%) showed no enhancement at all. Three masses (4.2%) appeared in the form of focal lesions in one of the lobes of pituitary gland showing washout on delayed contrast enhanced phase representing pituitary microadenoma, one (1.4%) appeared isointense on both T1WI & T2WI, showing intense post contrast enhancement suggestive of meningioma, one (1.4%) showed up as predominantly cystic, not showing enhancement representing craniopharyngioma and two (2.8%) showed convexity of upper margin of pituitary gland and its enlargement suggestive of pituitary hyperplasia. On MRI examination, pituitary macroadenoma was seen in 64 patients. Fifty-one (71.8%) patients were married and twenty patients (28.2%) were unmarried. Seven (10%) patients were nulliparous.

**Table 1:** *Contingency table.*

| | | HISTOPATHOLOGY | | TOTAL |
|---|---|---|---|---|
| | | Positive | Negative | |
| MRI | Positive | 62 (TP) | 2 (FP) | 64 |
| | Negative | 2 (FN) | 5 (TN) | 07 |
| Total | | 64 | 7 | 71 |

Histopathology results showed that 64 (90.1%) patients had pituitary macroadenoma. Results showed that overall 62(87.3%) were true positive, 5 (7.0 %) were true negative, 2 (2.8%) were false positive and 2 (2.8%) were false negative (Table 1). Results showed that sensitivity was 96.9% , specificity was 71.4% , positive predictive value (PPV) was 96.9%, negative predictive value (NPV) was 71.4% and accuracy of dynamic contrast MRI in detecting pituitary macroadenoma was 94.3% (Table 2).

**Table 2:** *Sensitivity, specificity, PPV, NPV and accuracy of MRI in detecting pituitary macroadenoma*

| | |
|---|---|
| Sensitivity (TP/ TP+FN) | 96.9% |
| Specificity (TN/ TN + FP) | 71.4% |
| Positive predictive value (TP / TP+ FP) | 96.9% |
| Negative predictive value (TN/ TN + FN) | 71.4% |
| Accuracy (TP+TN/ TP+TN+TN+FP) | 94.3% |

Percentages of the patient's presenting symptoms and involvement of adjacent structures are described below (Table 3 and Table 4).

**Table 3:** *Presenting symptoms in patients undergoing MRI for pituitary macroadenoma.*

| Sr # | SYMPTOMS | No. of Patients And Percentage |
|---|---|---|
| 1 | Headache | 67 (94.4%) |
| 2 | Visual disturbance | 51 (71.8%) |
| 3 | Increased prolactin levels | 34 (47.9%) |
| 4 | Menstrual irregularity | 30 (42.3%) |
| 5 | Galactorrhea | 28 (39.4%) |

**Table 4:** *MRI findings in patients of pituitary macroadenoma.*

| Sr # | MRI FINDINGS | No. of Patients And Percentage |
|---|---|---|
| 1 | Involvement of internal carotid artery | 51 (71.8%) |
| 2 | Presence of sellar floor depression | 48 (67.6%) |
| 3 | Optic chiasm compression | 46 (64.8%) |
| 4 | Compression of third ventricle | 42 (59.2%) |
| 5 | Extension into sphenoid sinus | 26 (36.6%) |
| 6 | Cavernous sinus invasion | 11 (15.5%) |

## Discussion:

In the relevant clinical setting of malfunctioning pituitary gland, visual abnormalities, or cranial nerve involvement, imaging of the pituitary gland is essential[11]. Radiologists and endocrinologists can now study the pituitary gland in immense detail due to recent improvement in neuroimaging [12]. MRI represents the standard imaging modality at the present time in the evaluation of normal pituitary gland, sellar and suprasellar structures due to its better contrast resolution and ability to obtain a dynamic assessment of contrast enhancement in pituitary tissue, which is an important factor in the recognition of pituitary adenomas[2]. When MRI is contraindicated due to pacemakers or intra cranial/ intra orbital metallic then CT scan is preferred, however, two disadvantages of CT are radiation and less soft tissue contrast that restrict the common use of CT scan in detecting pituitary masses. Now a days, MRI is the investigation of choice for pituitary lesions because of its multiplanar capability, magnetic field and lack of radiation exposure risk as well as higher soft tissue differentiation. MRI also provides relevant information about the composition and consistency of pituitary adenomas as well as correlation of gland with adjoining anatomical structures including optic chiasm, cavernous sinus, internal carotid artery, sphenoid sinus and ventricles which helps in planning management[12].It contributes to determining the best surgical approach and reducing postoperative complications[13].

In our study most common findings were hyperintense signal intensity mass on T2WI, involvement of internal carotid artery as well as sellar floor depression. Most common presenting complaints were headache and visual disturbances. Young female patients presented with galactorrhea and hormonal imbalance. Our aim was to find a non-invasive diagnostic modality which is as accurate as histopathology so that results of both can be compared. In a study carried out in 2018 on 33 patients, the findings are consistent with our study. The common presenting symptoms were headache and dimness of vision. The study showed consistency of lesions as solid to predominantly solid, mostly heterogeneously hyperintense on T2WI, and hypo to isointense on T1WI with immense post contrast

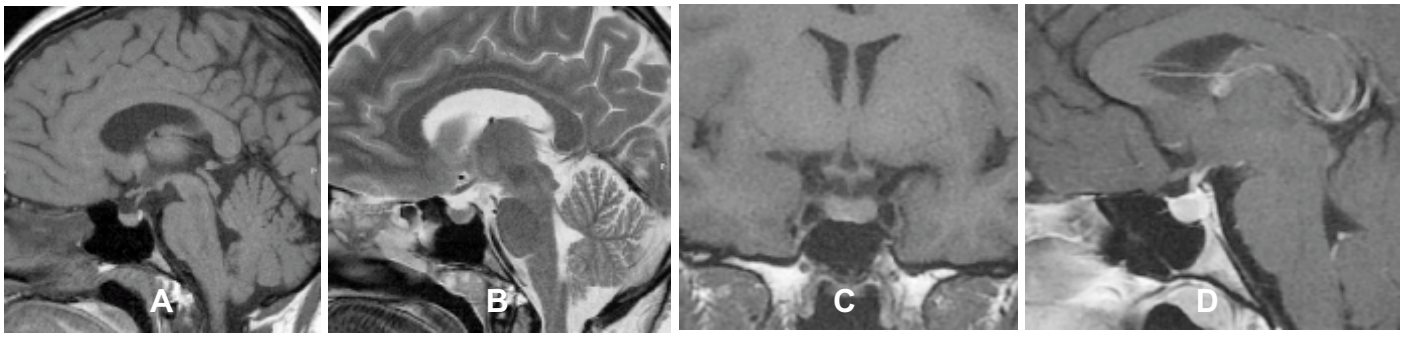


**Figure 1:** *Sagittal T1WI and T2WI multi echo multiplanar spin-echo (SE), 3 mm slice thickness sequence (A) at 1.5T showing normal anatomy of the pituitary gland (a,b). Coronal 3D T1 fast spin echo (FSE) 4 mm slice thickness sequence (c) showing optimal visualization of pituitary stalk and optic chiasm. Sagittal image showing homogenous parenchymal enhancement after intravenous administration of gadolinium (d).*

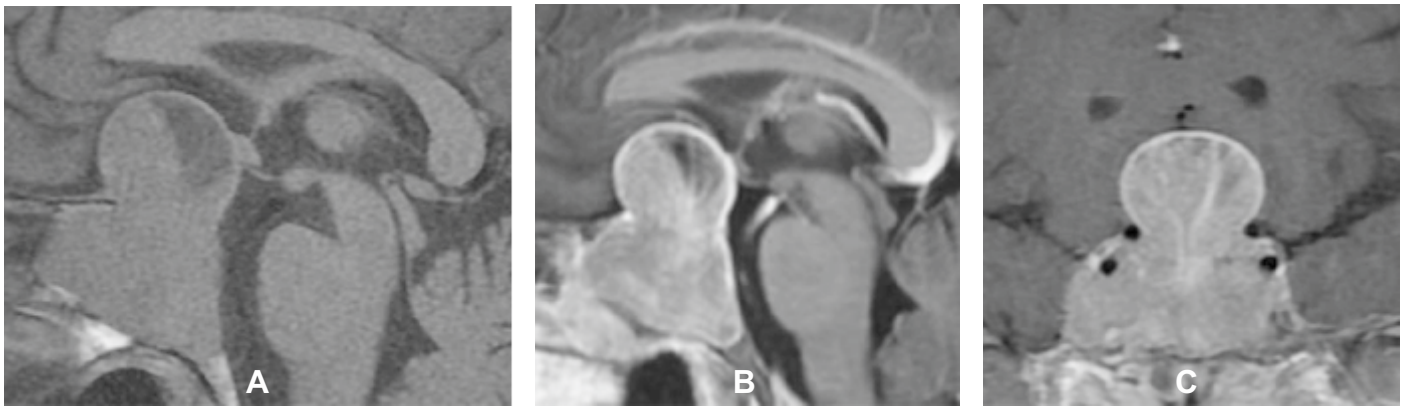


**Figure 2:** *Sagittal pre contrast T1WI multi echo multiplanar spin-echo (SE) 4 mm slice thickness sequence (a), Sagittal and coronal T1WI SE at 1.5T scanner, both performed after administration of contrast medium, showing inhomogeneous solid mass involving sellar and supra sellar region giving snowman sign, encasing right internal carotid artery with extension into sphenoid sinus, likely referable to macroadenoma (b,c).*

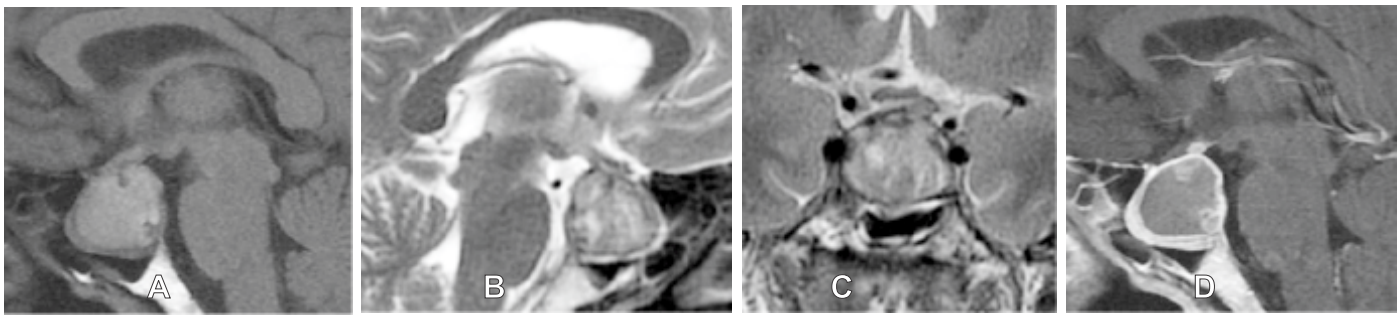


**Figure 3:** *Sagittal pre contrast T1WI multi echo multiplanar spin-echo (SE) 4 mm slice thickness sequence showing sellar and supra sellar mass having hyperintense signals representing hemorrhage (apoplexy) (a), sagittal and coronal T2WI SE at 1.5T scanner having T2WI hyperintense signals (b,c), Sagittal T1WI SE performed after administration of contrast medium, showing solid mass involving sellar and supra sellar region giving snowman sign stretching the optic chiasma and showing peripheral post contrast enhancement (d).*

enhancement[14]. In another study, presentation was dominated by headache, visual disturbance, and hypopituitarism[15].A similar study was conducted by Hemminki, Försti, and Ji. They were able to find relationship between sex and age for pituitary adenomas. Upto 30 years of age, Incidence rate was higher in female than males after which incidence rate increased in males. More noticeable symptoms of

associated hyperprolactinemia leading to amenorrhea and galactorrhea in females were the reason for early presentation[16]. In our study more cases were seen in females than males.

A similar study was carried out by Pouyan Femini et al. in 2011, where they compared pituitary MRI results with histopathological diagnosis keeping it as gold standard. They concluded that pituitary MRI had sensitivity of 99% and specificity of 29%. Four MRI reports were false negative and 15 were false positive. Twenty-one pathological reports revealed normal pituitary tissue[17] Our study results are similar to these published studies. Another descriptive study was conducted in 2013 in which one hundred and two patients (102) were studied. The pathological results determined 67 cases of microadenomas, 20 cases of macroadenomas and 15 cases of normal pituitary[18]. In a study carried out by Kim DJ et al, upon radiological examination, 32 (36%) of 88 patients showed pituitary apoplexy[19]. In our study eight masses (11%) contained hemorrhage.

However, our study had some limitations. Firstly, we lost few patients on follow up as elective surgery at our hospital was stopped due to COVID 19 pandemic. Results could have been more reliable and reproducible if the surgeries were performed here as well. Secondly, although we had included 101 patients in our study but few of the patients were not operated upon due to small size of mass and absence of mass effect reducing our sample size.

In our present study, sensitivity was found to be 96.9%, specificity was 71.4%, positive predictive value (PPV) was 96.9%, negative predictive value (NPV) was 71.4% and accuracy of dynamic contrast MRI in detecting pituitary macroadenoma was 94.3%.

## Conclusion:

MRI is a reliable and non-invasive imaging modality that allows the detection of pituitary macroadenoma with high sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. respectively. This study revealed the most common presenting symptoms, those patients who were operated upon due to visual disturbance, mass effect and then followed up. Along with these we found out involvement of adjacent structures including optic chiasma, cavernous sinus, third ventricle and sphenoid sinus which was only possible with MRI.

**Ethical Approval:** Given

**Conflict of Interest:** The authors declare no conflict of interest.

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## References:

1. Barkhoudarian G, Kelly DF. The pituitary gland: Anatomy, physiology, and its function as the master gland. In: Cushing's Disease. Elsevier; 2017. p. 1–41.
2. Varrassi M, Cobianchi Bellisari F, Bruno F, Palumbo P, Natella R, Maggialetti N, et al. High-resolution magnetic resonance imaging at 3T of pituitary gland: advantages and pitfalls. Gland Surg. 2019;8(Suppl 3):208–15.
3. Davies BM, Carr E, Soh C, Gnanalingham KK. Assessing size of pituitary adenomas: a comparison of qualitative and quantitative methods on MR. Acta Neurochir (Wien). 2016;158(4):677–83.
4. Tortora F, Negro A, Grasso LFS, Colao A, Pivonello R, Splendiani A, et al. Pituitary magnetic resonance imaging predictive role in the therapeutic response of growth hormone-secreting pituitary adenomas. Gland Surg. 2019;8(Suppl 3):150–8.
5. Zieliński G, Sajjad EA, Maksymowicz M, Pękul M, Koziarski A. Double pituitary adenomas in a large surgical series. Pituitary. 2019;22(6):620–32.
6. Basari R, Srivastava VK, Vasenwala S, Ansari H. Pituitary adenoma: A case report with special emphasis on approach to diagnosis. Clin Cancer Investig J. 2014;3(3):264.
7. Seig EP, Stepanyan H, Payne R, Ouyang T, Be Z. Vanishing Pituitary Macroadenoma: A Case Report. Cureus. 2016;8(10):e838.
8. Sen R, Sen C, Pack J, Block KT, Golfinos JG, Prabhu V, et al. Role of high-resolution dynamic contrast-enhanced MRI with golden-angle radial sparse parallel reconstruction to identify the normal pituitary gland in patients with macroadenomas. AJNR Am J Neuroradiol. 2017;38(6):1117–21.
9. Pepeira S, Vernekar JA, Amate SS, Cacogdar JA, Vernekar AJ. Magnetic Resonance Imaging in Evaluation of Pituitary Adenomas. International Journal of Anatomy. 2016;5(3):1-5.
10. Azeemuddin M, Naqi R, Wasay M. A descriptive study to

find possible correlation between MRI findings of pituitary gland and serum prolactin level. J Pak Med Assoc. 2013;63(6):739–42.

11. Ouyang T, Rothfus WE, Ng JM, Challinor SM. Imaging of the pituitary. Radiol Clin North Am. 2011;49(3):549–71,
12. Chaudhary V, Bano S. Imaging of the pituitary: Recent advances. Indian J Endocrinol Metab. 2011;15(Suppl 3):216-23.
13. Wang M, Liu H, Wei X, Liu C, Liang T, Zhang X, et al. Application of reduced-FOV diffusion-weighted imaging in evaluation of normal pituitary glands and pituitary macroadenomas. AJNR Am J Neuroradiol. 2018;39(8):1499-504.
14. Gupta K, Sahni S, Saggar K, Vashisht G. Evaluation of clinical and magnetic resonance imaging profile of pituitary macroadenoma: A prospective study. J Nat Sci Biol Med. 2018;9(1):34.
15. Chen L, White WL, Spetzler RF, Xu B. A prospective study of nonfunctioning pituitary adenomas: presentation, management, and clinical outcome. J Neurooncol. 2011;102(1): 129–38.
16. Hemminki K, Försti A, Ji J. Incidence and familial risks in pituitary adenoma and associated tumors. Endocr Relat Cancer. 2007;14(1):103–9.
17. Famini P, Maya MM, Melmed S. Pituitary magnetic resonance imaging for sellar and parasellar masses: ten-year experience in 2598 patients. J Clin Endocrinol Metab. 2011;96(6):1633–41.
18. Wenqiang Z, Jian Y, Yuanjun C. Diagnose pituitary adenoma using dynamic enhanced MRI: a quantitative approach. Chinese Journal of Medicine. 2015;95(23): 1837–41.
19. Kim D-J, Song Y-J, Kim S-J, Park M-K, Choi S-S, Kim K-U. Pituitary hemorrhage: classification and related factors. J Korean Neurosurg Soc. 2009;46(1):23–30.