

MRI BRAIN FINDINGS IN PATIENTS WITH HIGH SERUM PROLACTIN LEVELS

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ABSTRACT

Objective: The purpose of the study was to find MRI findings in patients with Prolactin levels above 1000mIU/L.

Methodology: This Retrospective study was conducted in Radiology Department, Rehman Medical Institute, Peshawar, from December 2009 to October 2012. A total of 86 patients, aged 16-48 years with high Prolactin levels, were screened with MRI for pituitary gland abnormalities. Only new undiagnosed patients were considered for the study. Children and patients with known causes for hyperprolactinaemia were excluded.

Results: The most common abnormality on MRI was microadenoma (n=34, 39.5%) followed by macroadenoma (n=14, 16.3%). 12(7%) cases of complete/partial empty sella syndrome were seen. Macroadenoma was more common in males (n=6 out of 14, 42.3%) while microadenoma was more common in females (n=32 out of 72, 44.4%).

Conclusion: Majority of Patients had an abnormal MRI finding, showing that MRI screening should be recommended for Prolactin levels above 1000mIU/L. Microadenoma was the most common abnormality, having higher incidence in female patients.

Key Words: Hyperprolactinaemia, Prolactin, MRI screening, Microadenoma, Macroadenoma.

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INTRODUCTION

Hyperprolactinaemia can be caused by excess production of Prolactin from pituitary gland adenoma, or by disturbance of feedback mechanism e.g., compression of the pituitary stalk or reduced dopa-

mine levels 1.

A serum Prolactin level <500 mIU/L for women and < 450 mIU/L for men is considered normal. High Prolactin levels of 1000-5000 mIU/L can be due to many reasons but levels greater than 5000 mIU/L are usually due to Macroadenoma. Although no studies are available in Pakistan for prevalence of hyperprolactinaemia, foreign studies estimate prevalence to be about 0.4% in a normal adult population. It could be as high as 9-17% in women with reproductive disorders. The causes of hyperprolactinaemia fall into three general categories: Physiologic, Pharmacologic and Pathologic¹.

Magnetic resonance imaging (MRI) scan of the pituitary gland is performed after physiologic causes, drug-induced and condition like secondary hyperprolactinaemia are ruled out^{2,3}. Pathologic hyperprolactinaemia may be due Microadenoma, Macroadenoma and empty sella syndrome (partial or complete). Empty sella syndrome may be primary i.e when a defect in the membrane covering the pituitary gland allows fluid in and presses on the pituitary gland resulting in its flattening or shrink-

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age. Secondary empty sella syndrome occurs due to a tumour or irradiation⁴. MRI is considered the most sensitive test for detecting pituitary tumors. MRI scans can determine the size of the tumors; it can also be used periodically to assess tumor progression/regression and the effects of chemotherapy. Computed Tomography (CT scan) can also be used, but it is less sensitive than the MRI for pituitary imaging⁵.

The purpose of this study was to determine the imaging findings in undiagnosed patients with high prolactin levels of above 1000 mIU/L and to find the correlation between Prolactin levels and pituitary findings using Magnetic resonance imaging (MRI).

METHODOLOGY

This Retrospective (descriptive) study was conducted in the Radiology Department of Rehman Medical Institute Peshawar, from December 2009 to October 2012. Magnetic Resonance Imaging (MRI) was done for 86 selected patients aged 16 to 48 years.

Serum Prolactin levels were measured in the laboratory of our institution. Only symptomatic patients were referred for serum Prolactin levels. Both undiagnosed male and female with serum Prolactin levels higher than 1000 mIU/L with no known cause for high Prolactin levels, were included in this study. Physiologic causes associated with hyperprolactinaemia like pregnancy and lactation were excluded in all patients. No patients were using any drugs associated with hyperprolactinaemia. Patients already diagnosed with pituitary disease were also excluded from the studies. Paediatric age group was also not included in this study.

Magnetic resonance imaging (MRI) findings were noted, MRI was interpreted by our radiologist working in the Department of Radiology at the Rehman Medical Institute Peshawar.

Correlation between serum Prolactin levels, age, sex and MRI finding were noted. MRI findings were grouped as Normal, Microadenomas, Macroadenomas, Complete empty sella syndrome and Partial empty sella syndrome.

SPSS 16.0 was used for data analysis, Pearson chi square was used as statistical test for testing the significance of data. A P value of <0.05 was considered statistical significant.

RESULTS

Out of 86 patients included in this study, 72 (83.7%) were females while 14 (16.3%) were males.

The age ranged from 16-48 years with, Mean of 30.16 and Standard Deviation of 8.883. 26 (30.2%) patients were aged 16-24 years, 26 (30.2%) patients were aged 25-30 years, 12 (14.0%) patients were aged 31-36 years, 14(16.3%) patients were aged 37-42 years and 8(9.3%) patients were between 43-48 years of age.

Patients with Prolactin level above 1000 mIU/L were included in the study. The Prolactin levels are shown in Table 1.

Out of 86 MRIs, 26 (30.2%) were normal, 34 (39.5%) showed microadenoma, 14(16.3%) showed macro adenoma, 6 (7%) showed empty sella syndrome and 6 (7%) showed partially empty sella syndrome.

Table 1: Prolactin levels

Prolactin levels (mIU/L)	Number of patient	Percent
1000 – 2000	48	55.8
2001 – 3000	14	16.3
3001 – 4000	16	18.6
4001 – 5000	6	7.0
5001+	2	2.3
Total	86	100.0

There was no significant relationship between age and Prolactin levels.

Most of the MRI reports were normal with Prolactin levels under 2000 mIU/L. With rising Prolactin levels, the percentage of macroadenomas increased and at a level above 5000 mIU/L, only macroadenomas were noted. The relationship between MRI reports and Prolactin levels is shown in Table 2.

Relationship between Sex of patient and MRI report is shown in Figure 1. In females most common abnormality was microadenoma. Nearly half of

the MRI reports of male patients were normal, with rest of them having macroadenoma. Complete/partial empty sella syndrome was only found in female Patients.

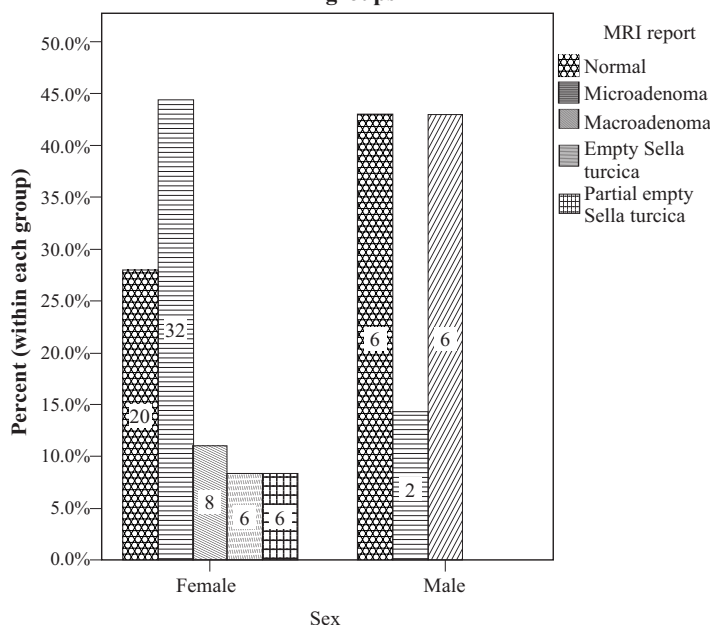
DISCUSSIONS

Patients aged between 16 and 48 years were included in this study. Majority of the patients were females, probably due to the fact that abnormal Prolactin levels manifest endocrine symptoms in females at much lower levels⁶. The female patients mostly presented in younger age group while males

Table 2: Relationship between MRI reports and Prolactin levels

Prolactin levels (mIU/L)	MRI findings					Total
	Normal	Micro-adenoma	Macro-adenoma	Complete Empty Sella Syndrome	Partial empty Sella Syndrome	
1000- 2000	22 (45.8%)	14 (29.2%)	6 (12.5%)	6 (12.5%)	0 (0%)	48
2001- 3000	4 (28.6%)	4 (28.6%)	2 (14.3%)	0 (0%)	4 (28.6%)	14
3001- 4000	0 (0%)	12 (75.0%)	2 (12.5%)	0 (0%)	2 (12.5%)	16
4001- 5000	0 (0%)	4 (66.6%)	2 (33.3%)	0 (0%)	0 (0%)	6
5001+	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	2
Total	26	34	14	6	6	86

Figure 1: Cluster bar graph showing MRI findings in male and female sex groups



presented mostly in older age. However, the Prolactin levels didn't show any significant relationship with the age of the patients.

Most of the patients having abnormally high Prolactin level (1000mIU/L or more) had some sort of abnormality on MRI. An increasing percentage of abnormal finding was seen with increase in Prolactin levels. This shows that 1000 mIU/L is a useful cutoff level for MRI screening. It is thus recommended that patients with Prolactin levels of above 1000mIU/L should go for an MRI screening. This has also been previously recommended in studies conducted elsewhere^{7,8}.

The most common abnormal finding was microadenoma (n=34), which was much more common than macroadenoma (n=14), this finding is also in agreement with previous studies conducted elsewhere^{9,10}. The other MRI findings were that of partial empty sella syndrome (n=6) and complete empty sella syndrome (n=6).

Most of the patients with normal MRI finding were having Prolactin levels of less than 2000 mIU/L, while there were no normal MRI reports in patients with Prolactin levels above 3000 mIU/L. This was in agreement with other studies^{9,11,12}. The normal patients who presented with abnormally high Prolactin levels, most likely had the condition called Macroprolactinaemia, as all other causes of hyperprolactinaemia were excluded before including them in the study. This has been reported elsewhere also 7.

Microadenoma was the most common abnormal finding in patients with elevated Prolactin levels. The percentage of microadenoma progressively decreased with increasing Prolactin levels while that of macroadenoma increased, such that above 5000mIU/L only macroadenomas were found. This was an expected finding, as increasing amount of Prolactin indicates a much larger adenoma, which is most of the times a macroadenoma^{13,14}. However, a clear direct relationship of Prolactin levels with the type of adenoma was not observed, this could be due the reason that some microadenomas are more efficient at producing Prolactin or in some cases a particular iso form of Prolactin "macroprolactin" is secreted by them, giving a high Prolactin level and hence symptomatology⁹.

Cases of partial empty sella syndrome and complete empty sella syndrome were also found in the study. Those patients had Prolactin levels between 1000-4000mIU/L. This could be probably due to re-

sidual Microadenoma¹⁵. All Cases of partial empty sella syndrome and complete empty sella syndrome in this study were of female patients¹⁶.

Most of the abnormal MRI findings were found in females while males had mostly a normal MRI report. The most common abnormal finding in females was microadenoma while in case of males the most common abnormality was macroadenoma (Figure 1) The reason for this could be the presentation of symptoms; in females small increase in Prolactin levels due to microadenoma can present with endocrine system related symptoms; in males however, unless a macroadenomas present with symptoms like visual problems or pressure effects, they rarely seek out a doctor¹⁷. This is a finding found in studies done elsewhere as well¹⁸⁻²⁰.

CONCLUSION

Majority of Patients had an abnormal MRI finding, showing that MRI is useful diagnostic tool and should be employed for patients with high Prolactin levels, once other causes for hyperprolactinaemia are excluded. A level of 1000mIU/L is a useful cut-off level for MRI screening. The most common finding was microadenoma followed by a macroadenoma. Microadenoma was more common in females while macroadenoma was common in males.

REFERENCES

1. Biller BM, Luciano A, Crosignani PG, Molitch M, Olive D, Rebar R, et al. Guidelines for the diagnosis and treatment of hyperprolactinemia. *J Reprod Med* 1999; 44: 1075-84.
2. Melmed S, Jameson JL. Disorders of the anterior pituitary and hypothalamus. In: Harrison's principles of internal medicine. 17th ed. New York: McGraw Hill Medical; 2008.
3. Casanueva FF, Molitch ME, Schlechte JA, Abs R, Bonert V, Bronstein MD, et al. Guidelines of the pituitary society for the diagnosis and management of prolactinoma. *Clin Endocrinol (Oxf)* 2006; 65: 265-73.
4. Melmed S, Kleinberg D, Ho K. Pituitary physiology and diagnostic evaluation. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM, editors. *Williams's textbook of endocrinology*. 12th ed. Philadelphia, PA: Saunders Elsevier; 2011.
5. Kulkarni MV, Lee KF, McArdle CB, Yeakley JW, Haar FL. 1.5-T MR imaging of pituitary

- microadenomas: technical considerations and CT correlation. *AJNR Am J Neuroradiol* 1988; 9: 5-11.
6. Vroonen L, Jaffrain-Rea ML, Petrossians P, Tamagno G, Chanson P, Vilar L, et al. Prolactinomas resistant to standard doses of cabergoline: a multicenter study of 92 patients. *Eur J Endocrinol* 2012; 167: 651-62.
 7. Bayrak A, Saadat P, Mor E, Chong L, Paulson RJ, Sokol RZ. Pituitary imaging is indicated for the evaluation of hyperprolactinemia. *Fertil Steril* 2005; 84: 181-5.
 8. Smith MV, Laws ER. Magnetic resonance imaging measurements of pituitary stalk compression and deviation in patients with nonprolactin-secreting intrasellar and parasellar tumors: lack of correlation with serum prolactin levels. *Neurosurgery* 1994; 34: 834-9.
 9. Hauche O, Rocha AJ, Maia ACM, Maciel RMB, Vieira JGH. Screening for macroprolactinaemia and pituitary imaging studies. *Clin Endocrinol (Oxf)* 2002; 57: 327-31.
 10. Rand T, Kink E, Sator M, Schneider B, Huber J, Imhof H, et al. MRI of microadenomas in patients with hyperprolactinemia. *Neurorad* 1996; 38: 744-6.
 11. Tamaki N, Yonezawa K. Prolactin producing adenoma. *Nihon Rinsho* 1993; 51: 2685-90.
 12. Colao A, Ferone D, Lastoria S, Cerbone G, Di Sarno A, Di Somma C, et al. Hormone levels and tumour size response to quinagolide and cabergoline in patients with prolactin-secreting and clinically non-functioning pituitary adenomas: predictive value of pituitary scintigraphy with 123I-methoxybenzamide. *Clin Endocrinol (Oxf)* 2000; 52: 437-45.
 13. Corsello SM, Ubertini G, Altomare M, Lovicu RM, Migneco MG, Rota CA, et al. Giant prolactinomas in men: efficacy of cabergoline treatment. *Clin Endocrinol (Oxf)* 2003; 58: 662-70.
 14. Ciccarelli E, Camanni F. Diagnosis and drug therapy of prolactinoma. *Drugs* 1996; 51: 954-65.
 15. Swanson JA, Sherman BM, Van Gilder JC, Chapler FK. Coexistent empty sella and prolactin-secreting microadenoma. *Obstet Gynecol* 1979; 53: 258-63.
 16. De Marinis L, Bonadonna S, Bianchi A, Maira G, Giustina A. Primary empty sella. *J Clin Endocrinol Metab* 2005; 90: 5471-7.
 17. Lafferty AR, Chrousos GP. Pituitary Tumors in Children and Adolescents. *J Clin Endocrinol Metab* 1999; 84: 4317-23.
 18. Farooq K, Malik TG, Rashid A. Pituitary macroadenomas: demographic, visual, and neuroradiological patterns. *Professional Med J* 2010; 17: 623-7.
 19. Care RH, Sunkaraneni VS, Theaker J, Harries PG. Rapidly progressing giant invasive prolactinoma. *J Laryngol Otol* 2012; 126: 840-3.
 20. Semple P, Fieggen G, Parkes J, Levitt N. Giant prolactinomas in adolescence: an uncommon cause of blindness. *Childs Nerv Syst* 2007; 23: 213-7.

CONTRIBUTORS

SG supervised the whole project, helped in the data analysis and final review of the manuscript. MN helped in data analysis, study design and interpretation of results. MZIK, MA, SHA, AK, SMN & MUK helped in data collection, data entry, writing and reviewing the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.