

Research Article

Hyperprolactinemia and macroprolactinemia in patients presenting with diabetic nephropathy

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ABSTRACT:

Background: In diabetes mellitus and chronic renal failure, prolactin secretion is disturbed. In the pathology of diabetic nephropathy progression, the role of prolactin remains undetermined.

Objective: To assess frequency of hyperprolactinemia and macroprolactinemia in patients presenting with diabetic nephropathy

Materials and methods: Study design: Cross section study. **Setting:** East Medical Ward, Department of Medicine, Mayo Hospital, Lahore. **Data collection procedure:** Fasting blood sample was drawn from each patient and sent to the laboratory of the hospital. Reports were assessed to measure prolactin level and macroprolactin level. If levels will be high then hyperprolactinemia and macroprolactinemia was labeled.

Results: Mean age of patients was 61.31 ± 11.63 years. There were 75(45.5%) males and 90(54.5%) females. Mean duration of diabetes was 5.85 ± 2.81 years. Mean duration for diabetic nephropathy was 5.45 ± 2.84 months. Hyperprolactinemia was seen in 43(26.1%) patients and macroprolactinemia in 21(12.7%) patients.

Conclusion: The frequency of Hyperprolactinemia and macroprolactinemia was although not that much higher in patients with diabetic nephropathy. Thus, the management which can slow the onset of diabetic nephropathy and its further progression is urgently required to enhance the quality of life & survival in these patients.

Key words: Hyperprolactinemia, Macroprolactinemia, Diabetic nephropathy

INTRODUCTION

In the chronic renal failure and diabetes mellitus, prolactin secretion is disturbed. In the pathology of diabetic nephropathy progression, the role of prolactin remains undetermined.

⁴Prolactin levels are raised in decreased kidney function. Prolactin level contributed significantly and independently to explain the variability of kidney function and Prolactin levels which were directly related with endothelial dysfunction and high risk of cardiovascular morbidity and mortality in two cohorts of Chronic Kidney Disease patients.⁵

So much studies showed that prolactin levels in diabetic patients were much increased.¹ One

study has reported that among type II diabetic nephropathy patients, hyperprolactinemia and macroprolactinemia were detected in 17% and 5.5% patients, respectively.⁶

The basic reason of our study was to assess the frequency of hyperprolactinemia and macroprolactinemia in patients presenting with diabetic nephropathy. Literature has reported that among cases of diabetic nephropathy, the magnitude of hyperprolactinemia are high. But there is no local evidence available in this regard which can help us in implementing the use of early screening of diabetic nephropathy patients to plan timely management protocols or

prevention in case of slight disturbance to prevent the patient from hazardous outcome i.e. CKD and hemodialysis. So we want to conduct this study to get local evidence which can be applicable in future. The results of our study will help a lot to improve knowledge and will guide the patients to plan the more appropriate management and preventive plan to prevent the patients from hazardous events after diabetic nephropathy along with hyperprolactinemia and macroprolactinemia.

OBJECTIVE

To assess the frequency of hyperprolactinemia and macroprolactinemia in patients presenting with diabetic nephropathy

MATERIAL AND METHODS:

STUDY DESIGN: Cross section Study

SETTING: At East Medical Ward, Department of Medicine, Mayo Hospital, Lahore

DURATION OF STUDY: 6 months i.e. from 01-03-2016 to 30-08-2016

SAMPLE SIZE: Of 165 cases calculated with confidence level 95%, margin of error 3.5% and taking expected percentage of macroprolactinemia i.e. 5.5% in patients presenting with diabetic nephropathy.

Sampling Technique: Technique was non-probability & consecutive sampling

SAMPLE SELECTION:

INCLUSION Criteria: Patients aged 40 – 80 years of either sex who presented with diabetic nephropathy. It was defined as :

- Patients with persistent Albuminuria (>300mg/d) confirmed on medical record for ≥ 1 month
- Patients with progressive decline in the glomerular filtration rate < 90 mL/min/1.73 m²
- Patients of diabetes (BSF > 126 mg/dl) confirmed on medical record diagnosed at

least 1 month ago

Exclusion Criteria: Patients with co-morbid conditions i.e. chronic renal failure, respiratory disorder like asthma or COPD, history of smoking and alcohol drinker, prolactinoma, hypothyroidism (TSH > 5 IU/L), Pregnancy and breast feeding, acromegaly, epilepsy and cushing disease.

Data Collection Procedure: Total 165 patients who fulfilled the inclusion criteria were selected from Out Door Patient Department. Demographic information was also obtained. Then fasting blood sample was collected from each patient through a disposable sterile syringe with the assistance of a staff nurse under strict aseptic conditions. All samples were sent to the laboratory of the hospital. Reports were assessed to measure prolactin level and macroprolactin level by using Electrochemiluminescence method through PEG precipitation assay. If levels will be high then hyperprolactinemia (level of serum prolactin > 25 μ g/L for women, and > 20 μ g/L for men) and macroprolactinemia ($\geq 50\%$ macroprolactin in serum) was labeled. All this information was recorded on proforma.

DATA ANALYSIS:

The obtained information was entered and analyzed through SPSS version 21. Hyperprolactinemia and macroprolactinemia was calculated as frequency and percentage.

RESULTS

Mean age of patients was 61.31 \pm 11.63 years. There were 75 (45.5%) males and 90 (54.5%) females. There were 44 (26.7%) patients BMI was normal, 49 (29.7%) were underweight, 38 (23%) were overweight and 34 (20.6%) were obese. Mean duration of diabetes reported by patients was 5.85 \pm 2.81 years. Table 1
Hyperprolactinemia was seen in 43 (26.1%) patients and macroprolactinemia was seen in 21 (12.7%) patients. Table 2

Table-1: Demographics of patients

N	165
Age (years)	61.31±11.63
Gender (M:F)	75: 90
BMI	
Normal	44 (26.7%)
Under Weight	49 (29.7%)
Over Weight	38 (23%)
Obese	34 (20.6%)
Duration of diabetes (years)	5.85±2.81
Duration of diabetic nephropathy (months)	5.45±2.84

Table-2: Frequency of Hyperprolactinemia & Macroprolactinemia

	Frequency (%)
Hyperprolactinemia	
Yes	43(26.1%)
No	122(73.9%)
Macroprolactinemia	
Yes	21(12.7%)
No	144(87.3%)

DISCUSSION

Circulating levels of the pituitary hormone PRL usually do not exceed 20 ng/mL, except in pregnant or nursing women and, of course, in diseased states. The classical disease that leads to high PRL levels is prolactinoma, in which lactotropic tumor cells in the pituitary autonomously produce PRL. Another pathologic situation in which PRL levels rise is CKD. In patients with CKD, there appears to be an abnormal regulation of PRL secretion which features PRL hypersecretion, the failure of dopamine to suppress PRL levels, and a blunted PRL response to stimulatory agents including chlorpromazine, thyrotropin releasing hormone, vasoactive intestinal polypeptide, arginine, and insulin hypoglycaemia.⁸⁻¹⁰ Also, in the presence of CKD, the physiological oscillations of serum PRL levels diminish, and the circadian rhythm of PRL secretion progressively disappears.¹¹

In this study mean age of patients was 61.31±11.63 years. There were 75(45.5%) male and 90(54.5%) female patients included in the study. Mean duration of diabetes reported by patients was 5.85±2.81 years. However mean duration for diabetic nephropathy was 5.45±2.84 months. Hyperprolactinemia was seen in 43(26.1%) patients and macroprolactinemia was seen in 21(12.7%) patients. Both

Hyperprolactinemia and macroprolactinemia did not show any statistically significant association with age, gender, BMI, duration of diabetes and duration of nephropathy. One study has reported that among type II diabetic nephropathy patients, hyperprolactinemia and macroprolactinemia were detected in 17% and 5.5% patients, respectively.⁶ Bahaa Al-Trad in her study reported that in the model of development of experimental diabetic kidney disease, there is raised renal secretion of PRL-R. It suggests a very important role for prolactin in the onset and progression of kidney injury secondary to diabetes mellitus.¹²

Recently in 2015 Jakob Triebel and his team members in their study reported that patients with Diabetes Mellitus and decreased renal function showed a high urinary Prolactin excretion. Urinary Prolactin excretion in the context of proteinuria may contribute to prolactin dysregulation in renal insufficiency. In their results they also reported that patients with Diabetes Mellitus and renal impairment had significantly higher urine PRL levels than patients with Diabetes Mellitus and normal renal function and control patients.¹ In diabetic patients, studies reported that prolactin levels were high.¹ However no studies in recent times have addressed the role of prolactin in

diabetic nephropathy. There exists some evidence to support the role of prolactin in the diabetic nephropathy. Raised serum PRL levels in diabetic nephropathy is correlated negatively with glomerular filtration rate and positively with serum creatinine concentration.¹³

Additionally, Mejía-Rodríguez et al. have reported that bromocriptine, a type-2 dopamine receptor agonist, reduced prolactin levels and thus prevented the progression of chronic kidney disease in type 2 diabetics.¹⁴ However as per observation of Bahaa Al-Trad in their study, a positive association between serum prolactin level and renal PRL-R mRNA expression supports the concept that the higher level of PRL may contribute to the up-regulation of renal PRL-R mRNA in the diabetic patients kidney.¹² Although, no data is available, however nephro-protective effects of bromocriptine have been also observed in CKD patients with type 2 diabetes mellitus.¹⁴ Patients with Diabetes Mellitus and concomitant renal impairment demonstrate an altered renal metabolic clearance of PRL that leads to an increase of PRL levels in urine. High PRL levels show that they have in diabetes prevalence¹⁵, diabetic retinopathy, and diabetic nephropathy, mechanisms of renal metabolic clearance of PRL deserve investigation.^{1, 16, 17}

CONCLUSION

The frequency of hyperprolactinemia and macroprolactinemia was although not that much higher in patients with diabetic nephropathy. Management might delay the onset of diabetic nephropathy and its progression is urgently required to improve quality of life and survival of diabetic patients.

REFERENCES

1. Arnold E, Rivera JC, Thebault S, Moreno-Páramo D, Quiroz-Mercado H, Quintanar-Stéphano A, et al. High levels of serum prolactin protect against diabetic retinopathy by increasing ocular vasoinhibins. *Diabetes* 2010;59(12):3192-7.
2. Rathi M, Ramachandran R. Sexual and gonadal dysfunction in chronic kidney disease: Pathophysiology. *Indian J Endocrinol Metab* 2012;16(2):214.
3. Mejía-Rodríguez O, Herrera-Abarca JE, Ceballos-Reyes G, Avila-Diaz M, Prado-Uribe C, Belio-Caro F, et al. Cardiovascular and renal effects of bromocriptine in diabetic patients with stage 4 chronic kidney disease. *BioMed Res Int* 2013;2013.
4. Al-Trad B. Prolactin receptor mRNA expression in experimental diabetic nephropathy: Relationship with urinary albumin excretion. *Neuroendocrinol Letters* 2015;36(6):552-6.
5. Carrero JJ, Kyriazis J, Sonmez A, Tzanakis I, Qureshi AR, Stenvinkel P, et al. Prolactin levels, endothelial dysfunction, and the risk of cardiovascular events and mortality in patients with CKD. *Clin J Am Soc Nephrol* 2012;7(2):207-15.
6. Sari F, Sari R, Ozdem S, Sarikaya M, Cetinkaya R. Serum prolactin and macroprolactin levels in diabetic nephropathy. *Clin Nephrol* 2012;78(1).
7. Wolf G. New insights into the pathophysiology of diabetic nephropathy: from haemodynamics to molecular pathology. *European journal of clinical investigation* 2004;34(12):785-96.
8. Triebel J, Moreno-Vega AI, Vázquez-Membrillo M, Nava G, García-Franco R, López-Star E, et al. High Prolactin Excretion in Patients with Diabetes Mellitus and Impaired Renal Function. *Clinical laboratory* 2015;61(7):709-16.
9. Arnaout MA, Hamzeh YS, Ajlouni KM. Prolactin responses to vasoactive intestinal polypeptide and thyrotropin releasing hormone in chronic renal failure. *Acta endocrinologica* 1991;125(6):651-6.
10. Schmitz O, Møller J. Impaired prolactin response to arginine infusion and insulin hypoglycaemia in chronic renal failure. *Acta endocrinologica* 1983;102(4):486-91.
11. Biasioli S, Mazzali A, Foroni R, D'Andrea G, Feriani M, Chiaramonte S, et al. Chronobiological variations of prolactin

- (PRL) in chronic renal failure (CRF). *Clinical nephrology* 1988;30(2):86-92.
12. Al-Trad B. Prolactin receptor mRNA expression in experimental diabetic nephropathy: Relationship with urinary albumin excretion. *Neuroendocrinology Letters* 2015;36(6):552-6.
 13. Sari F, Sari R, Ozdem S, Sarikaya M, Cetinkaya R. Serum prolactin and macroprolactin levels in diabetic nephropathy. *Clinical nephrology* 2012;78(1):33-9.
 14. Mejía-Rodríguez O, Herrera-Abarca JE, Ceballos-Reyes G, Avila-Diaz M, Prado-Uribe C, Belio-Caro F, et al. Cardiovascular and renal effects of bromocriptine in diabetic patients with stage 4 chronic kidney disease. *BioMed research international* 2013;2013.
 15. Wang T, Lu J, Xu Y, Li M, Sun J, Zhang J, et al. Circulating prolactin associates with diabetes and impaired glucose regulation. *Diabetes care* 2013;36(7):1974-80.
 16. Triebel J, Macotela Y, de la Escalera GM, Clapp C. Prolactin and vasoinhibins: endogenous players in diabetic retinopathy. *IUBMB life* 2011;63(10):806-10.
 17. Triebel J, Huefner M, Ramadori G. Investigation of prolactin-related vasoinhibin in sera from patients with diabetic retinopathy. *European Journal of Endocrinology* 2009;161(2):345-53.