ORIGINAL RESEARCH PAPER

Volume-7 | Issue-8 | August-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EPIDEMIOLOGICAL EVALUATION OF PARATHYROID HORMONE IN UROLITHIASIS

Urology

Neeraj Agarwal — Associate Professor, Dept. of urology and renal transplant, SMS Hospital and Medical college, Jaipur, Rajasthan, India.

Ashish Gupta* — Senior Resident, Dept. of urology and renal transplant, SMS Hospital and Medical college, Jaipur, Rajasthan, India. *Corresponding Author

Vinay Tomar — Senior Professor and Head of Department, Dept. of urology and renal transplant, SMS Hospital and Medical college, Jaipur, Rajasthan, India.

S S Yadav — Senior Professor , Dept. of urology and renal transplant, SMS Hospital and Medical college, Jaipur, Rajasthan, India.

Shivam Priyadarshi — Senior Professor, Dept. of urology and renal transplant, SMS Hospital and Medical college, Jaipur, Rajasthan, India.

ABSTRACT

Background: Hyperparathyroidism has been reported to account for as many as 5-8% of all calcium stone formers. Around 15-21 % patients will have renal calculi as their presenting complaints. Aim of this study is to identify the metabolic derangement in association with PTH hormone in patients of urolithiasis.

Methods: All patients with urolithiasis(renal and/or ureteric) were evaluated for parathyroid hormone. Patients were divided in two groups – group A (with normal PTH level = 4.7-114 pg/ml) and group B (with raised PTH = >114pg/ml). Patients with raised creatinine(>1.6), known case of hyperparathyroidism and those who refused for PTH evaluation were excluded from study.

Results: Total of 230 patients were available for analysis out of which 22 patients had raised PTH. PTH was significantly raised in recurrent (p=.02), staghorn calculi (p=.01) and with stone burden >2.5cm.

Conclusions: Ours is probably the 1st study to evaluate ureteric calculi and stone burden in association to raised PTH. Young age, Bilateral, recurrent and larger stones are more prone to have raised PTH.

KEYWORDS

Pth, Urolithiasis, Staghorn Calculi

INTRODUCTION:

Hyperparathyroidism in India is largely a symptomatic disease and due to lack of screening and awareness most patients presents late in the course of disease when systemic symptoms appears.[1-2] Hyperparathyroidism has been reported to account for as many as 5-8% of all calcium stone formers.[3] Around 15-21 % patients will have renal calculi as their presenting complaints.[4-5] Other presentations are hyper-calcemic crisis, bone disease, neuromuscular dysfunction, abdominal pain, psychiatric symptoms etc.[6] Renal calculi in this group of patients are generally seen as bilateral, multiple, staghorn, and recurrent stones if left undiagnosed or untreated.[7] Biochemical analysis in stone formers though well accepted but is not widely practiced. Aim of this study is to identify the metabolic derangement in association with PTH hormone in patients of urolithiasis.

MATERIALS AND METHODS:

The study was conducted in the Department of Urology, SMS MEDICAL COLLEGE AND ATTACHED HOSPITALS. All patients with urolithiasis(renal and/or ureteric) admitted to urology department from October 2016 to March 2017 were evaluated for parathyroid hormone. Patients were divided in two groups – group A (with normal PTH level = 4.7-114 pg/ml) and group B (with raised PTH = >114pg/ml).

Patients with raised creatinine(>1.6), known case of hyperparath yroidism and those who refused for PTH evaluation were excluded from study. Statistical analysis was done with SPSS software version 22 wherever necessary.

RESULTS:

Total of 230 patients were available for analysis out of which 22 patients had raised PTH. Both groups were compared with respect to age and sex. Patient's demographic data were as shown in figure 1 and table 1.

Table 1 showing demographic data

Variables	Group A	Group B	P value
Age (mean ± SD)	38.6 ±15.7	31.9 ±18.2	.06
Gender			
Male	140	13	-
Female	68	9	-

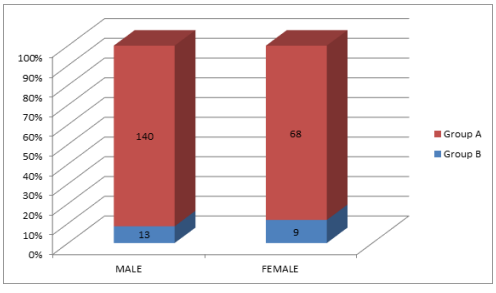

Figure 1 showing demographic data.

Association of raised PTH with stone location was also analysed. Statistically significant correlation was present with bilateral stones(p<.01) (either b/l renal or uretric or renal + uretric) whereas renal and ureteric locations per se were not significant as shown in table 2.

Table 2 showing association with location.

Location	Group A (n=208)	Group B (n= 22)	P value
Renal	122 (58.66%)	7 (31.81%)	.22
Ureteric	57 (27.4%)	4 (18.19%)	.61
Bilateral	29 (13.94%)	11 (50%)	.0034
Total	100%	100%	

On further evaluation for association with stone characteristics it was found that PTH was significantly raised in recurrent (p=.02), staghorn

calculi (p=.01) and with stone burden >2.5cm as shown in table 3.

Table 3 showing association with stone characteristics.

Stone characteristics	Group A (208)	Group B (22)	P value
Recurrent stones	20	7	.02
Large and Staghorn * calculi	22	8	.01
Stone burden (cm)	1.91 ± .84	2.51 ±1.38	.005
* stones in two or more than two calyces.			

In serum biochemical analysis, mean calcium and PTH(4.7-114 pg/ml) were 9.2±1.29 and 161±40 in group B which was significant (p = .0005 and <.001 respectively), as shown below in table 4.

Table 4 showing serum biochemical analysis.

STUDY POPULATION	GROUP A	GROUP B	P VALUE
CALCIUM (8.5-10.5mg/dl)	8.6 ±.68	9.2 ±1.29	.0005
PTH (4.7-114pg/ml)	52.25 ±23.53	161±40	<.001
PHOSPHOROUS(2.5-4.5mg/dl)	3.16 ±.69	3.18 ±1.35	0.94
URIC ACID(2.5-7.7mg/dl)	5.0 ± 1.19	5.8 ± 1.5	.003

DISCUSSION: Although there is enough literature on renal manifestations in hyperparathyroidism but the vice versa is not true. The mean age of presentation in elevated PTH group was 31.9 years which is in accordance as reported by Pradeep PV et al[1] and Shah VN et al[2]. Male to female ratio in group B was 1.44:1 which was similar to others[3,8,9]. Hyperparathyroidism has been reported to account for as many as 5-8% of all calcium stone formers.[3] Around 15-21 % patients will have renal calculi as there presenting complaints.[4-5] In our study we found that 22(9.5%) out of 230 patients of urolithiasis had raised PTH which is far less than what was found by AD Bhar et al[3] (28%) but higher than Pak CY et al[10] (2-3%) . The possible explanation is strict inclusion criteria by Bhar et al in which they included only cases with bilateral, recurrent or large unilateral calculi patients whereas in our study we included all cases irrespective of size, location and presentation.

Ours is the 1st study to assess ureteric calculi in association with raised PTH. Interestingly the prevalence of raised PTH was comparable in ureteric calculi and renal calculi in our study. This reflects that even ureteric calculi are not immune to raised PTH and requires subsequent evaluation just as renal calculi. Bilateral calculi whether renal or ureteric or renal plus ureteric were more prone to have raised PTH(27.5%) that is also statically significant (p<.01) and in concordance with Miller et al[11].

On evaluation 27 recurrent cases 7(25.5%) had raised PTH which is statically significant and comparable to 21% as was found by Bhansali et al[5]. Stone recurrence is important history to seek hyperparathyroidism as causative disease as shown by other studies[3,5,12]. C L Mollerup[13] and L Rejnmark[14] also showed that risk of nephrolithiasis was increased 10 years before surgery, and risk of recurrence became normal more than 10 years after parathyroid surgery in HPT.

On further study of association with stone burden raised PTH was present in 8 out of 30 patients of large and staghorn calculi which was statistically significant as also shown by AD Bhan[3] and Bhansali et al[5]. Mean stone size in raised PTH group was >2.5cm which was significantly larger than group A 1.91cm (p= .005). In a retrospective analysis of 271 hyperparathyroid patients done by Suh et al[15] they found 7% incidence of asymptomatic renal calculi out of which 21% patients had stone size >10mm as seen by sonography.

In biochemical analysis serum calcium was significantly higher in group B which is in concordance with Corbetta[8] and Parks[16], however others have found no difference in stone forming and non-stone forming hyperparathyroidism[9,13,17,18] . D'Angelo[19] found an inverse relation of serum calcium in stone former and non-stone former HPT. Serum phosphorus was similar in both groups as seen by Silverberg[17]. Elevated level of uric acid in group B was also significant(p=.003), which shows direct relationship of uric acid with urolithiasis and raised PTH as shown by K-Y Chin et al[20] and Yamamoto[21].

There are some limitations in our study. Firstly, confirmation of hyperparathyroidism by sestamibi scan was not done in our study due to lack of diagnostic facilities at our centre. Secondly, stone analysis was not performed. Thirdly, general population for control was not taken. Lastly, 24 hour urinary analysis was also not done.

In conclusion, ours is probably the 1st study to evaluate ureteric calculi and stone burden in association to raised PTH. Young age, Bilateral, recurrent and larger stones are more prone to have raised PTH. Similarly patients with raised serum calcium and uric acid are also at risk of raised PTH. Ureteric calculi have similar risk of raised PTH as renal calculi, so they too should be evaluated in a similar fashion. Further well designed multi-intitutional trials are required to confirm our results and overcome our limitations.

References

1. Pradeep PV, Jayashree B, Mishra A, Mishra SK. 10. Systematic review of primary hyperparathyroidism in India: the past, present, and the future trends. Int J Endocrinol 2011; 2011 : 921814.
2. Shah VN, Bhadada SK, Bhansali A, Behera A, Mittal BR, 7. Vadera B. Influence of age and gender on presentation of symptomatic primary hyperparathyroidism. J Postgrad Med 2012; 58 : 107-11.
3. Anita Dhar Bhan, V. R. Minocha, Sanjay Gupta. Urolithiasis : Screening for Hyperparathyroidism is Essential. JK science Vol. 3 No.4, October-December 2001.
4. Gopal RA, Acharya SV, Bandgar T, Menon PS, Dalvi AN, Shah NS. Clinical profile of primary hyperparathyroidism from western India: A single center experience. J Postgrad Med 2010;56:79-84.
5. Bhansali A, Masoodi SR, Reddy KS, Behera A, das Radotra B, Mittal BR, et al. Primary hyperparathyroidism in north India: A description of 52 cases. Ann Saudi Med 2005;25:29-35.
6. Mundy GR, Cove DH, Fisken R. Primary hyperparathyroidism 2. changes in the pattern of clinical presentation. Lancet 1980;1 : 1317-20.
7. Leela et al. Renal manifestations of primary hyperparathyroidism. Indian Journal of Endocrinology and Metabolism / Mar-Apr 2012 / Vol 16 | Issue 2
8. Corbetta S, Baccarelli A, Aroldi A, Vicentini L, Fogazzi GB et al. Risk factors associated to kidney stones in primary hyperparathyroidism. J Endocrinol Invest 28:122–128; 2005
9. Odvina CV, Sakhaee K, Heller HJ, Peterson RD, Poindexter JRet al. Biochemical characterization of primary hyperparathyroidism with and without kidney stones. Urol Res 35: 123–128; 2007
10. Pak CY, Peters P, Hurt G, Kadesky M, Fine M, Reisman D, et al. Is selective therapy of recurrent nephrolithiasis possible? Am J Med. 1981 Oct;71(4):615-22
11. MILLER, A. and MITCHELL, J. P. (1952), HYPERPARATHYROIDISM AND RENAL CALCULI. British Journal of Urology, 24: 91–98. doi:10.1111/j.1464-410X.1952.tb04666.x
12. Brardi S, Duranti E (2016) Nephrolithiasis Associated with Normocalcemic or Hypercalcemic Primary Hyperparathyroidism: An Update on Medical Management. Arch Renal Dis Manag 2(1): 013-018. DOI: 10.17352/2455-5495.000010
13. Charlotte L Mollerup, Peter Vestergaard, Vibe Geds¯ Fr¯kjÊr, Leif Mosekilde, Peer Christiansen et al. Risk of renal stone events in primary hyperparathyroidism before and after parathyroid surgery: controlled retrospective follow up study. BMJ VOLUME 325 2002
14. Lars Rejnmark, Peter Vestergaard, and Leif Mosekilde. Nephrolithiasis and Renal Calcifications in Primary Hyperparathyroidism. J Clin Endocrinol Metab 96: 2377–2385, 2011
15. Suh JM, Cronan JJ, Monchik JM 2008 Primary hyperparathyroidism: is there an increased prevalence of renal stone disease?AJRAmJ Roentgenol 191:908–911
16. Joan H. Parks, Fredric L. Coe, Andrew P. Evan* and Elaine M. Worcester. Clinical and laboratory characteristics of calcium stone-formers with and without primary hyperparathyroidism. B J U I N T E R N A T I O N A L 2008| 1 0 3 , 6 7 0 – 6 7 8 | doi: 10. 11 11 /j. 1464-410X.2008.08064.x
17. Silverberg SJ, Shane E, Jacobs TP, Siris ES, Gartenberg F et al. 1990 Nephrolithiasis and bone involvement in primary hyperparathyroidism. Am J Med 89:327–334
18. So¨ reide JA, van Heerden JA, Grant CS, Lo CY, Ilstrup DM 1996 Characteristics of patients surgically treated for primary hyperparathyroidism with and without renal stones. Surgery 120:1033–1037;discussion 1037–1038
19. D'Angelo A, Lodetti MG, Giannini S, Castrignano R, al Awady M,et al Hyperparathyroidism: cause or consequence of recurrent calcium nephrolithiasis? Miner Electrolyte Metab1992 18:359–364
20. Chin K-Y, Ima Nirwana S, Wan Ngah WZ. Significant association between parathyroid hormone and uric acid level in men. Clinical Interventions in Aging. 2015;10:1377-1380. doi:10.2147/CIA.S90233.
21. YAMAMOTO, S., HIRAISHI, K., NAKAMURA, S. and GHAZIZADEH, M. (1987), Serum and Urinary Uric Acid in Primary Hyperparathyroidism. British Journal of Urology, 59: 386–389. doi:10.1111/j.1464-410X.1987.tb04831.x