

Follow up of Patients with Parathyroid Adenoma Detected by Parathyroid Scan

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ABSTRACT

Background: Primary hyperparathyroidism (PHPT) is the third most endocrine disorder after diabetes and thyroid disease. The objective of this study was to observe the outcome of those patients who had positive parathyroid scan with Technetium-99m (99mTc) sestamibi scan referred to National Institute of Nuclear Medicine & Allied Sciences (NINMAS) to perform parathyroid scan.

Patients and Methods: This longitudinal observational type of study was carried out at NINMAS, from January 2016 to December 2016. A total number of 43 hyperparathyroid patients who had positive parathyroid scan were included in this study during one year follow up period. Their clinical status, biochemical profile & treatment history were evaluated. Chi-square and paired t-test were used to analyze the variables.

Results: Among 43 study patients, number of male patients was 26 (60.5%) and female patients were 17 (39.5%). The mean \pm SD age was 42.44 ± 12.11 years and majority was in age group 41-50 years. It was observed that 40 (93.0%) patients were symptomatic and only 3 (7.0%) were asymptomatic. Regarding symptoms, majority (81.4%) patients had bone pain followed by renal stone (58.1%). More than half (55.8%) patient had abdominal pain or cramps. Twenty nine (67.4%) patients undergone operation and 14 (32.6%) patients did not receive operative treatment at the one year follow up period.

Among 43 patients 29 (67.4%) were operated and all operated patients relieved their symptoms whereas patients 14 (32.6%) had not undergone operation and their symptoms persisted. There was strong statistical significant association ($P < 0.05$) between operation and relief of symptoms. The biochemical profile of study patients showed that preoperative mean serum calcium level was 10.92 ± 2.85 mg/dl which reduced after operation (7.53 ± 2.75 mg/dl). The mean value of serum parathyroid hormone (PTH) level also reduced from 748 ± 744.77 pg/ml to 171.61 ± 168.23 pg/ml.

Conclusion: Among all patients, 67.4% received operative treatment and were relieved from symptoms at one year follow up. Significant number of hyperparathyroid patients (32.6%) failed to receive operative treatment due to poor economic condition. More awareness is needed among physicians and patients about immediate operative treatment to alleviate their sufferings as well as to avoid crippling complications.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the third most endocrine disorder after diabetes and thyroid disease (1). Primary hyperparathyroidism is a disease characterized by excessive secretion of parathyroid hormone (PTH), an 84-amino acid polypeptide hormone which is regulated directly by the plasma concentration of ionized calcium (2). It is now recognized as a spectrum ranging from inappropriately high or even normal PTH in the setting of high-normal or even normal calcium (1). Ninety-five percent of PHPT cases are sporadic. Of these cases, 75–85% result from a single adenoma, 2–12% result from double adenomas, 10–15% result from multiple gland hyperplasia, and <1% result from parathyroid carcinoma (1-3).

Over the last several decades, its clinical presentation in most populations has shifted from florid symptomatic disease to mostly that of an asymptomatic one (4). PHPT occurs more commonly in women and the onset before 50 years of age is rare. In postmenopausal age the relationship between man and woman changes from 1:3 to 1:5 (2). PHPT is more likely to present with skeletal complications, or nephrolithiasis. (2,5)

Combined 99mTc-sestamibi and 99mTc scintigraphy with SPECT is now routinely performed preoperatively in developed countries with a sensitivity of 79 % and a positive predictive value of 91 % (6). The positive parathyroid scan of hyperparathyroid patients are not routinely followed up at NINMAS. Outcome of those positive patients with or without surgery are not evaluated. Evaluation of

follow up studies has major impact on their treatment and further decision making. Events of disease outcome with or without surgery in patients of PHPT in Bangladesh are not elaborately evaluated yet in our socio economic context. The information and follow up events will enrich our knowledge to manage hyperparathyroid patients. In this regard, follow up study of parathyroid adenoma with parathyroid positive scans at NINMAS has been designed to evaluate the outcome of the patients to observe how many patients are receiving operative treatment and to observe cure rate and alleviation of the symptoms.

PATIENTS AND METHODS

This longitudinal observation study was performed at NINMAS, Dhaka during January, 2016 to December, 2016. Prior to commencement of this study, approval had been taken from Medical Research Ethics Committee (MREC), NINMAS. All the patients included in the study were informed about the procedure and written consent was taken. Proper permission was taken from the concerned department and institute.

A total 43 hyperparathyroid patients with previous positive parathyroid scan were collected from medical records of NINMAS and recalled them. Sample technique was purposive. Inclusion criteria were hyperparathyroid patients with positive scan and exclusion criteria were patients with other endocrine diseases and also with secondary and tertiary hyperparathyroidism.

Detailed history was taken. Biochemical tests like PTH, serum calcium level & inorganic phosphate were performed pre and post operatively. In these patients, parathyroid scan was done by ^{99m}Tc sestamibi injecting 15-20 m Ci by intra venous route. Low energy high resolution collimator of gamma camera with window setting 20% at 140 KeV was used to detect parathyroid glands. Focal increased radiotracer uptake with visualization of thyroid gland in early image and still increased focal uptake in same

area without visualization or significant decreased thyroid uptake in delayed image suggest parathyroid adenoma.

In addition, ultrasound imaging of renal and parathyroid glands system were done and bone mineral density (BMD) were done in some cases. The collected data were compiled and analyzed using window based computer software MS Excel and Statistical Package for Social Science (SPSS-17) by appropriate statistical methods. Continuous data were presented as mean and standard deviation (SD). Categorical qualitative data were presented as percentage (%). Chi-square (χ^2) test was done for qualitative data. In each analysis, the level of significance was considered when P value < 0.05. Various tables were used for data presentation in different steps of research protocol.

RESULTS

Among 43 study patients, number of male patients was 26 (60.5%) and female patients were 17 (39.5%). The mean \pm SD age was 42.44 ± 12.11 years and majority was in age group 41-50 years. It was observed that 40 (93.0%) patients were symptomatic and only 3 (7.0%) were asymptomatic. Regarding symptoms, majority (81.4%) patients had bone pain followed by renal stone (58.1%). More than half (55.8%) patient had abdominal pain or cramps. Significant number of patients had complaints of fatigue (44.2%), muscle weakness (37.2%), pancreatitis (16.35%), bone fracture (11.6%) and few had palpable neck mass and chronic renal failure (2.3%). Twenty nine (67.4.0%) patients undergone operation and 14 (32.6%) patients did not receive operative treatment at the one year follow up period.

Among 43 patients 29 (67.4%) were operated and all operated patients relieved their symptoms whereas patients 14 (32.6%) had not undergone operation and their symptoms persisted. There was strong statistical significant association ($P < 0.05$) between operation and relief of symptoms. The biochemical profile of

study patients showed that preoperative mean serum calcium level was 10.92 ± 2.85 mg/dl which reduced after operation (7.53 ± 2.75 mg/dl). The mean value of serum parathyroid hormone (PTH) level also reduced from 748 ± 744.77 pg/ml to 171.61 ± 168.23 pg/ml.

Table 1 showed age & sex status of the study subject, it was observed that approximately one third (32.6%) patients belong to age 41-50 years followed by 25.6 % between 31 – 40 years.

Distribution of the patients by gender demonstrated that 26 (60.5%) of the patients were male & 17 (39.5) were female giving a male to female ratio of 1:0.65. The difference was not statistically significant ($P=0.05$) between age & gender.

Table 1: Distribution of the study subjects by age & Sex (n=43)

Age (in years)	Sex		Total (%)	P value
	Male (%)	Female (%)		
≤ 30	6 (14.0)	2 (4.7)	8 (18.6)	0.679
31-40	5 (11.6)	6 (14)	11 (25.6)	
41-50	8 (18.6)	6 (14.0)	14 (32.6)	
51-60	5 (11.6)	2 (4.7)	7 (16.3)	
>60	2 (4.7)	1 (2.3)	3 (7.0)	
Total	26 (60.5)	17 (39.5)	43 (100)	

Level of significance 0.05

Presence of symptoms in the study subjects, it was observed that 40 (93.0%) patient were symptomatic and only 3 (7.0) were asymptomatic (Table 2).

Table 2: Distribution of the study subject by symptoms (n=43)

Clinical feature	Number of Patients	Percentage
Symptomatic	40	93.0
Asymptomatic	3	7.0

Some patients received operative treatment and some patients failed to receive operative treatment; treatment status of the study subjects are depicted in Table 3.

Table 3: Distribution of patient by treatment status.

Operation status	Frequency	Percentage
Operated	29	67.4
Non operated	14	32.6
Total	43	100.0

Preoperative & post operative values of both serum calcium and serum PTH level were reduced but statistical significant association ($P>0.05$) was not found between preoperative & post operative values shown in Table 4.

Table 4: Preoperative & postoperative biochemical profile of study patients

Biochemical profile	Preoperative value (Mean±SD)	Postoperative value (Mean±SD)	P Value
Serum calcium level (mg/dl) (Normal value: 8.5-10 mg/dl)	10.92 ± 2.85	7.53 ± 2.75	0.000
Serum phosphate level (mg/dl) (Normal value: 3.5-5 mg/dl)	3.05 ± 1.82	Not done	-
Serum PTH (pg/ml) (Normal value: 11.0-65.0 pg/ml)	748 ± 744.77	171.61 ± 168.23	0.000
Serum Vit-D (ng/ml) (Normal value: >20 ng/ml)	20.63 ± 11.83	Not done	-

Level of significance 0.05

DISCUSSION

PHPT is the third most endocrine disorder after diabetes and thyroid disease due to excess secretion of PTH and disorder of calcium homeostasis. An estimated prevalence is 1% in the general population and prevalence is higher in adult after age of 50. Majority of patients are symptomatic and asymptomatic are rare in developing country.

This observational type of study was carried out with an aim to observe the outcome of the patients who have positive parathyroid scan at NINMAS with

without the surgery and also to create awareness about the benefits of surgery.

A total of 43 diagnosed patients with parathyroid adenoma who had positive parathyroid scan at NINMAS, Bangabandhu Sheikh Mojiib Medical University (BSMMU) campus during January 2016 to December 2016, were included in this study. Patients with history of secondary and tertiary hyperparathyroidism and other causes of hypercalcemia, pregnant and lactating mother were excluded from the study. The present study findings were discussed and compared with previously published relevant studies.

In a meta analysis, it had been shown that primary hyperparathyroidism mostly occurred in older age over 55 years than young. It is 2-3 times more frequently in women than in men and had a higher prevalence in postmenopausal women (2). It was observed in present study that approximately one third (32.6%) patients belong to age 41-50 years followed by 25.6 % between 31 – 40 years. The mean age of the patients was 42.44 ± 12.11 years and youngest and the oldest patients were 15 and 65 years respectively.

In India, Anil Bhansali et al. (7) had described that female are more suffered than male. Male female ratio is 1:3.3. In the present study it was observed that 26 (60.5%) of the patients were male & 17 (39.5%) were female and male to female ratio of 1:0.65. In this study gender demonstrates of male prevalence is higher than female due to lack of knowledge and socio-economical culture where male persons are more privileged.

About 80 percent of people with hyperparathyroidism have few or no symptoms. In these people, hyperparathyroidism is typically detected when a blood test was done for some other reason (8). Yu Kwang Donovan Tay et al. (4) had described on their study that, the clinical presentation of PHPT in most population has shifted from symptomatic diseases to

asymptomatic one. Symptoms are bone pain and renal pain mostly. In this present study, it was observed that most of the patients 40 (93.0%) were symptomatic and only 3 (7.0%) were asymptomatic. So, reverse situation exists in our context most of the patients were symptomatic.

Walgenbach S et al. (9) had described that classically PHPT targets the kidney, skeleton and mind. Complaints of the patients are fatigue, weakness, abdominal pain, bone pain followed by renal stone. In recent days, parathyroid adenoma is also elicited by screening tests for evaluation of symptoms (8,10). Similarly in this study that most of the cases; patients were evaluated to investigate symptoms related to other systems of the body.

Parathyroidectomy is the gold standard treatment of PHPT. There is no doubt about the PTX in Eastern and Western countries. Traditional neck exploration mostly practiced in the sub-continent but this traditional operation has changed to most directional operation or MIP. Parathyroidectomy is the only definitive treatment of PHPT (11). Symptomatic patients are expected to get more benefits from curative parathyroidectomy, and patients considered to be asymptomatic frequently report improvement in quality-of-life indexes. Rubin MR et al. (12) showed the same results. After PTX the operation success rate is very high and recurrence is very low.

In this study, it was observed among 43 patients 29(67.4%) went for parathyroidectomy operation and among them 27 were symptomatic. Their symptoms were relieved after operation. Whereas in 14 (32.6%) patients did not receive operative treatment. Among them 13 patients were symptomatic and their symptoms persisted. Strong statistically significant association ($P < 0.05$) between operation and relief of symptoms and no recurrence was found in this study.

The pre-operative mean serum calcium and PTH level were comparatively high but after operation reduction levels were marked (12).

In the present study, preoperative mean serum calcium level was 10.92 ± 2.85 mg/dl which was reduced after operation (7.53 ± 2.75 mg/dl). The mean value of serum PTH level was also reduced from preoperative 748 ± 744.77 pg/ml to postoperative 171.61 ± 168.23 pg/ml.

The limitation of the study was that all patients were retrospectively collected. Prospective study with large population may be considered to guide or counsel the patients to go for surgery without delay. Follow up period of study was short.

CONCLUSION

In this study, most of the patients were symptomatic 40 (93%) with chief complaints of bone pain 35 (81.4%). Among 43 parathyroid adenoma with positive ^{99m}Tc sestamibi scan 29 (67.4%) patients went for parathyroidectomy operation and they all were relieved from symptoms at one year follow up time. Remaining 14 (32.6%) patients did not take operative treatment. They were receiving symptomatic management and could not avail operative treatment due to financial problem. From this study, this may be concluded that significant number of hyperparathyroid patients failed to receive operative treatment in the context of poor economic condition. More awareness is needed among physicians and patients about immediate operative treatment to alleviate their sufferings as well as to avoid crippling complications.

REFERENCES

1. Madkhali Tariq, Amal Alhefdhi, Herbert Chen and Dawn Elfenbein. Primary hyperparathyroidism. *Ulus Cerrahi Derg* 2016;32(1):58–66.
2. Percivale A, Paola Gnerre, Giulio Damonte and Sandra Buscaglia. Primary Hyperparathyroidism: Epidemiology, Clinical Features, Diagnostic Tools and Current Management. *Italian J of Med* 2015;9(5):330–45
3. Alhefdhi A. Current Concepts in the Presentation, Diagnosis and Management of Primary Hyperparathyroidism. *J of Surgery* 2015;11(1):305–312
4. Yu Kwang Donovan Tay, Joan Khoo, and Manju Chandran. Surgery or no surgery: What works best for the kidneys in primary hyperparathyroidism? A study in a multi-ethnic Asian population. *Indian J Endocrinol Metab* 2016;20(1):55–61.
5. Rubin MR, Bilezikian JP, McMahon DJ, et al. The Natural History of Primary Hyperparathyroidism with or without Parathyroid Surgery after 15 Years. *The J of Clin Endocrinol Metab* 2008;93(9):3462–70.
6. Cheung K, Wang TS, Farrokhlyar F, Roman SA and Sosa JA. A meta-analysis of preoperative localization techniques for patients with primary hyperparathyroidism. *Ann Surg Oncol* 2012;19:577–835.
7. Bhanshali A, Masoodi SR, Reddy KS, Behera A, Das Radotra, Mittal BR et al. Primary Hyperthyroidism in North India: a Description of 52 Cases. *Ann Saudi Med* 2005;25(1):29–35.
8. Mazzagila PJ, Berber E, Kovach A, Milas M, Esselstyn C and Siperstein AE. The changing presentation of hyperparathyroidism over 3 decades. *Arch Surg*. 2008 Mar;143(3):260–66
9. Walgenbach S, Hommel G, Junginger T. Outcome after Surgery for Primary Hyperparathyroidism: Ten-year Prospective follow-up Study. *World J Surg* 2000;25(5):564–69.
10. Megan K A and David F S. Mild Primary Hyperparathyroidism: A Literature Review. *Oncologist* 2014;19(9):919–29.
11. Scott M Wilhelm, Tracy S. Wang and Daniel T Ruan. The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism. *JAMA Surg* 2016;151(10):959–68.
12. Rubin MR, Bilezikian JP, McMahon DJ, et al. The Natural History of Primary Hyperparathyroidism with or without Parathyroid Surgery after 15 Years. *The Journal of Clinical Endocrinology and Metabolism*. 2008;93(9):3462–70.