Original Research Article

DOI: http://dx.doi.org/10.18203/2349-2902.isj20170507

Prevalence of previously undiagnosed hypothyroidism in patients with cholelithiasis in a tertiary care center, North-East India

Debabrata Singha^{1*}, Naresh Manohar Pawar¹, Prabhu B. J.², Nitesh Kumar¹, Sankamithra Gopalarathnam¹

¹Department of General Surgery, ²Department of Radio-diagnosis, Silchar Medical College and Hospital, Silchar, Assam, India

Received: 27 January 2017 Accepted: 01 February 2017

*Correspondence: Dr. Debabrata Singha,

E-mail: drsinghadebabrata@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Earlier, the studies had an increased prevalence of previously diagnosed hypothyroidism in gallstone patient and recent studies also demonstrated low bile flow in hypothyroid subjects or the sphincter of oddi expresses thyroid hormone receptors and thyroxin has a direct prorelaxing effect on the sphincter. Iceberg of hypothyroidism was present in cholelithiasis patients. The objective of this study was to find out the prevalence of previously undiagnosed hypothyroidism in cholelithiasis patients.

Methods: A prospective study was conducted in the 500 consecutive patients with cholelithiasis between 1st October 2014 and 31st March 2016 to find relation between gallstone and hypothyroidism. Patients already diagnosed as hypothyroidism were excluded. In each patients, detailed history and clinical examination was done and sent for ultrasound of neck for goitre detection and laboratory Thyroid hormone assay (S-FT3, S-FT4 and S-TSH).

Results: A total of 2.2%, 5.0% and 6.6% (total 13.8%, 69 of 500) of the cholelithiasis patients were diagnosed to have clinical, subclinical and borderline subclinical hypothyroidism. In women older than 50 year, the prevalence of clinical and subclinical plus borderline-hypothyroidism was 6.8% and 25.6% ($11.7\%\pm13.9\%$) and clinical plus subclinical plus borderline-subclinical hypothyroidism was 32.4% in cholelithiasis patients.

Conclusions: Although a low prevalence of hypothyroidism was found in this study, but it is evident that subclinical and borderline subclinical hypothyroidism were significantly more common, compared with the clinical hypothyroidism and with increasing age there was increase in its prevalence, so we recommend that S-TSH level should be measured for every patient with cholelithiasis older than 50 years.

Keywords: Cholelithiasis, Goitre, Hypothyroidism, Thyroid hormone assay

INTRODUCTION

Gallstones are the most common biliary pathology, which can be divided into three main types: cholesterol, pigment (black, brown) or mixed stones. In the USA and Europe, 80% are cholesterol or mixed stones, where as in Asia, 80% are pigment stones. Cholesterol or mixed stones contain 51 - 99 % cholesterol plus admixture of calcium salts, bile acids, bile pigments and phospholipids. 1,2 Gallstones may be single or multiple, large or small.

Those containing calcium salts are radio opaque. Single stones are uncommon but usually consist mainly of cholesterol and arise due to a disorder of the physico-chemical equilibrium which normally maintains cholesterol in micelle form in the bile, small amount of cholesterol and traces of iron where detected. Amony studies were done to identify risk factor for biliary lithiasis. In the West, studies have focused on hypersaturation of cholesterol in bile in nucleation process as a critical step in the genesis of bile stone. For

decades, there has been a discussion, whether thyroid disorders can cause gallstone disease.

Particularly, there are several explanations for a possible relation between gallstone disease and hypothyroidism; these explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to change of composition of the bile.⁵ Recent studies also demonstrated low bile flow in hypothyroid subjects. Furthermore, the sphincter of oddi expresses thyroid hormone receptors and thyroxin has a direct pro-relaxing effect on the sphincter.^{5,6}

Both low bile flow and sphincter of oddi dysfunction are regarded as important functional mechanisms that may promote gallstone formation. The usage of thyroxin was even suspected to dissolve gallstones, however, a spontaneous passage of the stone to the duodenum could be excluded in this case report. In western countries 10-12% of adults develop gallstones. Process involving factors affecting bile content and bile flow. A crucial factor in the forming of bile duct stones is biliary stasis, which may be caused by sphincter of oddi stenosis, dyskinesia, or bile duct strictures. 11,12

The prevalence of previously undiagnosed thyroid function abnormalities has never been studied in gallstone patients before. If an increased prevalence of thyroid disorders will be found, it might have an effect on the diagnostic and therapeutic work up of patient with gallstone. Hypothyroidism is the most common cause of secondary hypercholesterolemia. Patients with hypothyroidism have serum level of cholesterol approximately 50% higher than level in Euthyroid patients and 90% of all hypothyroid patients have elevated cholesterol level. Here

METHODS

A prospective study was done in the 500 consecutive cholelithiasis patients between 1st October 2014 and 31st March 2016, detailed history and clinical examination including name, age, sex etc. and symptoms and signs of hypothyroidism including presence or absence of goitre will be taken. Investigations to be done in study include, neck ultrasound and level of S-FT3, S-FT4, and S-TSH.

Patients were divided according to history, clinical examination, ultrasound of the neck and thyroid hormones assay (S-FT3, S-FT4, S-TSH) into 4 groups;

- The symptom-free patients with S-TSH concentrations above the upper limit of the normal range (>6.0 mU/L) were considered as sub clinically hypothyroid.
- The symptom-free patients with S-TSH close to the upper limit of the normal range (5.0-6.0 mU/L) were considered as borderline sub clinically hypothyroid.

- The patients with symptoms of hypothyroidism with S-TSH level above the upper limit (>6.0 mU/L) and S-FT4 / S-FT3 level below the normal limit (<9.0 pm/L / <2.6 pm/L) were considered as clinically hypothyroid.
- Euthyroid group with clinical and thyroid hormones assay normal (S-TSH (0.2-4.5mU/L), S-FT4 (9–21pmol/L) and S-FT3 (2.6-6.2pmol/L)).

All these groups may present with or without goitre.

Statistical tool used were mean, median, mode, fisher's exact probability, x^2 text etc.

RESULTS

In this prospective study, 500 patients with cholelithiasis were randomly selected. 425 (85%) were females and 75 (15%) were males with median age was 43 years (range 24 - 68 years) and 38 years (30 - 63 years) respectively, as shown in Table 1.

Peak age of the patients in this study was between 40 - 50 years followed by 51 - 60 years and 31 - 40 years age groups, as shown in Figure 1.

Thyroid disorder in the form of hypothyroidism was found in 69 (13.8%) patients, all were females. Among them, 25 (5%) were diagnosed as subclinical hypothyroidism, 33 (6.6%) as subclinical borderline and 11 (2.2%) as clinical hypothyroidism. In women older than 50 year prevalence of clinical, subclinical and borderline-subclinical hypothyroidism was 6.8%, 11.7% and 13.9% respectively as shown in Table 2.

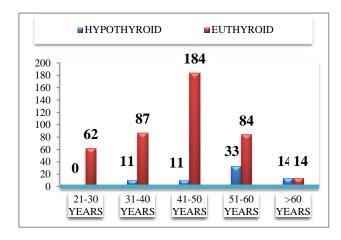


Figure 1: Number of cases of cholelithiasis in relation to age and thyroid function.

Among 69 hypothyroidism patients, in laboratory investigation we found that, 36 patients recorded with high S-TSH and low S-FT3, S-FT4, 24 patients with high S-TSH and low S-FT4 and 9 patients with high S-TSH and low S-FT3 as shown in Table 3.

Table 1: Distribution of patients of cholelithiasis in relation to gender, age and hypothyroidism.

Candan	No	Donomtooo	Age		Hypothyroid	lism	
Gender	No.	Percentage	Mean	Range	Clinical	SC	BSC
Male	75	15	38 years	30-63 years	Nil	Nil	Nil
Female	425	85	43 years	24-68 years	11	25	33
P≥0.05			Fisher's exact probability= 0.89				

Table 2. The prevalence of clinical, subclinical and subclinical borderline hypothyroidism and euthyroid in relation with cholelithiasis in different age groups and in total.

Age (years)	Clinical hypothyroid	SC hypothyroid	BSC hypothyroid	Total hypothyroid	Euthyroid	Total
21-30	0	0	0	0	62	62
31-40	0	3	8	11	87	98
41-50	1	5	5	11	184	195
51-60	7	10	16	33	84	117
>60	3	7	4	14	14	28
Total	11 (2.2%)	25 (5.0%)	33 (6.6%)	69 (13.8%)	431 (86.2%)	500 (100%)

 $X^2 = 50.6856$; p= 0.0001

Table 3: The levels of S-FT3, S-FT4 and S-TSH in 69 hypothyroid patients with cholelithiasis.

	No. of patients	High S- TSH	Low S-FT3	Low S-FT4	Low S-FT3 and S-FT4
Cholelithiasis with low S-FT3 and S-FT4	36	36	0	0	36
Cholelithiasis with low S-FT4	24	24	0	24	0
Cholelithiasis with low S-FT3	9	9	9	0	0
Total	69	69	9	24	36

Table 4: Thyroid enlargement in relation to Hypothyroidism and euthyroid, in patients with cholelithiasis.

Gender	Goitre		Non goitre	Total pages (9/)		
Gender	Euthyroid (%) Hypothyroid (%)		Euthyroid (%)	Hypothyroid (%)	Total cases (%)	
Female	2	12	354	57	425	
Male	0	0	75	0	75	
Total	2 (0.4%)	12 (2.4%)	429 (85.8%)	57 (11.4%)	500 (100%)	
P value	N.S.≥0.05	•	S=<0.05			

S/N.S: significant / not significant

From 500 cholelithiasis patients, 14 (2.8%) were found with goitre, 2 (0.4%) (according to the thyroid hormone assay) were euthyroid and 12 (2.4%) had hypothyroidism. Among 486 (97.2%) non-goiter patients 429 (85.8%) were euthyroid and 57 (11.4%) had hypothyroidism as shown in Table 4. From total number of hypothyroidism none was males and 69 were females F/M ratio found is 69:0.

DISCUSSION

In past decades, the studies have been shown that, there is an association between diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism, explained at least partly by the lack of prorelaxing effect of T4 on the sphincter of oddi contractility.¹⁵ We further investigated to find out the

prevalence of previously undiagnosed hypothyroid abnormalities in cholelithiasis patients.

The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting early thyroid failure is an increased TSH concentration. He we found an independent relation of high serum TSH levels with gallstones among females. Similar finding was found by Honore LH probably due to higher number of female patients in the study. He all said there is an independent relation of high serum TSH levels with gallstones among males, predominantly among those who had sonographically detected gallstones.

The majority of patients were in 40-50 years age group in our study, while in study done by Johanna L et al it was in women older than 60 years while in other study by Honore LH, and Inkinen J it was noted that high

gallstones prevalence was found in women > 65 years of age. This probably contributed to the sex hormonal imbalance at this age. ^{6,17,19}

In study done by Johanna L, the prevalence of subclinical hypothyroidism was 11.4% in gallstones and none of the patients were clinically hypothyroid.¹⁹ But in this study the prevalence of previously undiagnosed thyroid disorder in the form of hypothyroidism was found in 13.2% patients. Subclinical hypothyroidism was 5.0%, borderline subclinical hypothyroidism was 6.6% and clinical hypothyroidism was 2.2% in females. There was no hypothyroidism found in males with no clinically significant association between hypothyroidism and gallstones (p-value >0.05).

Volzke H in his study found that, there were (10.3%) patients with high TSH, which is approximately the same as in our study (13.8%) and (88.6%) with normal TSH which is approximately the same as this study (86.2%).¹⁸

In present study it was found that in the cholelithiasis patients, subclinical and borderline subclinical hypothyroidism are significantly more common, compared with the clinical hypothyroidism (11.6 vs. 2.2%; P value 0.0001) and the prevalence in the subgroup of women older than 50 year is high.

CONCLUSION

Although a low prevalence of previously undiagnosed hypothyroidism was found in this study, but it was evident that subclinical and borderline subclinical hypothyroidism were significantly more common, compared with the clinical hypothyroidism and with increasing age there was increase in its prevalence, so we recommend that, S-TSH level should be measured for every patient with cholelithiasis older than 50 years.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

institutional ethics committee

REFERENCES

- Russel RCG. The gall bladder and bile ducts. In: Williams NS, Bulstrode CJK, Oconnell PD. Bailey and Love's short practice of surgery, 25th edition. London, Edward Arnold Ltd. 2008:1119-20.
- 2. Yousif HH. Relationship between serum levels of TSH and cholesterol with types of gallstones. Iraqi Postgraduate Med J. 2011;10:7-12.
- 3. Bassi N, Aggio L, Ghiro S, Meggiato T, Mario DF, Favero DG. X-ray diffraction study of biliary calculi morphological and composition correlations of calculi. G Clin Med. 1990;71:331-5.

- Kleiner O, Ramesh J, Huleihel M, Cohen B, Kantarovich K, Levi C, et al. A comparative study of gallstones from children and adults using FTIR spectroscopy and fluorescence microscopy. BMC Gastroenterology. 2002;2:3.
- Cicala M, Hibib FI, Fiocca F, Pallotta N, Corazziari E. Increased sphincter of oddi basal pressure in patients affected by gallstone disease: a role of biliary stasis and colicky pain? Gut. 2001;48:414-7.
- Inkinen J, Sand J, Nordback I. Association between common bile duct stones and treated hypothyroidism. Hepato Gastroenterology. 2001;47:919-21.
- 7. Vassilakis JS, Nicolopoulos N. Dissolution of gallstones following thyroxine administration. A case report. Hepato Gastroenterology. 1981;28:60-1.
- Diehl AK. Epidemiology and natural history of gallstones disease. Gastroenterol Clin North Am. 1991;20:1-19.
- Heaton KW, Braddon FE, Mountford RA, Hugnes AO, Emmett PM. Symptomatic and silent gallstones in the community. Gut. 1991;32:316-20.
- Kartzar W, Mason RA, Kachele V. Prevalence of gallstones in sonographic surveys worldwide. J Clin Ultrasound. 1999;27:1-7.
- George L, Jordan J. Choledocholelithiasis. Curr Prob I Surg. 1982;19:722-98.
- Thistle JL. Pathophysiology of bile duct stone. World J Surg. 1998;22:1114-8.
- Osenes M, Lootveit T, Larsen S, Aune S. Duodenal diverticula and their relationship to age, sex and biliary calculi. Scand J Gastroenterology. 1981;16:103-7.
- 14. Bergman F, Linden VW. Further studies on the influence of thyroxin on gallstones formation in hamsters. Acta Chir Scand. 1966;131:319-28.
- Laukkarinen J, Sand J, Saaristo R, Salmi J, Turjanmaa V, Vehkalahti P, et al. Is bile flow reduced in patient with hypothyroidism? Surgery. 2003;133:288-93.
- 16. Woeber KA. Update on the management of hyperthyroidism and hypothyroidism. Arch Intern Med. 2000;160:1067-71.
- 17. Honore LH. A significant association between symptomatic cholesterol cholelithiasis and treated hypothyroidism in women. J Med. 1981;12:199-03.
- Volzke H, Robinson DM, John U. Association between thyroid function and gallstone disease. World J Gastroenterol. 2005;11:5530-4.
- Laukkarinen J, Kiudelis G, Lempinen M, Raty S, Pelli H, Sand J, et al. Increased prevalence of subclinical hypothyroidism in common bile duct stone patients. J Clin Endocrinol Metab. 2007;92:4260-4.

Cite this article as: Singha D, Pawar NM, Prabhu BJ, Kumar N, Gopalarathnam S. Prevalence of previously undiagnosed hypothyroidism in patients with cholelithiasis in a tertiary care center, North-East India. Int Surg J 2017;4:932-5.