Section: General Surgery

Original Research Article

A STUDY ON THE PREVALENCE OF HYPOTHYROIDISM IN DIAGNOSED CASES OF GALL BLADDER STONES

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Abstract

Background: Gallstone disease is on the rise in the Indian population. For decades there has been discussion whether thyroid disorders could cause gall stone disease. This study intends to show the prevalence of previously undiagnosed hypothyroidism in patients with gall stones. **Materials and Methods:** 102 patients with gallstone disease were selected by purposive sampling technique in MNR Medical College and Hospital between August 2020 and November 2022. Data related to the objectives of the study were collected. **Result:** Gallstone disease was common in the 31- 50 year age group. Cholelithiasis was more common in females (59.8%) in our study. Serum TSH was elevated in 15.7% of the cases predominantly in females. 6.86% of the patients had symptoms of hypothyroidism. **Conclusion:** The study concludes that patients with gallstones between 31-50 years should be checked for thyroid function test because of higher incidence of hypothyroidism among this age group as per our study.

INTRODUCTION

For decades, there has been a discussion, whether thyroid disorders could cause gallstone disease. Particularly, there are several explanations for a possible relation between hypothyroidism and gallstone disease. These explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to a change of the composition of the bile. The hypothyroidism can be either a subclinical type or hypothyroidism (overt) where the level of thyroxine is actually below normal. Subclinical hypothyroidism (mild thyroid failure) is identified when serum thyroid hormones are within normal lab level, but serum thyroid stimulating hormone (TSH) level is slightly raised.[1] However, some extra thyroidal effect of it has been reported.[2,3]

Since, Sandblom first proved the hormonal action of CCK (cholecystokinin) on the sphincter of Oddi, several other hormones have shown to affect sphincter of Oddi activity bile streams via the cystic duct to fill and unfill the gall bladder.

There are two physiologic mechanisms established in the gall bladder are mucosal absorption of water and electrolyte which concentrates the stored hepatic bile and smooth muscle contraction, which discharges gall bladder contents into the upper small intestine.[4]

Motility of gall bladder happens in the lack of food (inter-digestive period) and response to meals (digestive period), the last being subdivided into 4 phases according to the site of origin of stimulus: cephalic, gastric, intestinal and ileocolonic.[5]

The sphincter of Oddi plays a important role in guiding the bile flow into the gall bladder or the duodenum and inhibiting reflux of duodenal contents into the biliary tree.[6]

There are numerous clarifications for a possible relation between hypothyroidism (thyroid failure), and lipid metabolism and gall stone formation.

These descriptions include

1. Known link between thyroid failure and disturbance of lipid metabolism that may consequently lead to a change of composition of bile (Experimental in rabbit).[7]
2. Duodenum- Low bile flow in the hypothyroid state.[8]
3. Expression of thyroid hormone receptors of Sphincter of Oddi and thyroxine has a direct pro-relaxing effect on the sphincter of Oddi.[9] (Experimental in pig).
4. Thyroxine treatment in some cases has been suspected to dissolve gall stones and CBD stones.[10] (Case report)
5. There is dysmotility of digestive tract in hypothyroidism.[11]

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6. In various studies hypothyroidism has been linked with reduced bilirubin excretion due to decreased activity of UDP glucoronyl transferase.[12]

Recent studies also demonstrated low bile flow in hypothyroid subjects. Furthermore, the sphincter of Oddi (SO) expresses thyroid hormone receptors and thyroxine has a direct pro- relaxing effect on the sphincter. Both low bile flow and sphincter of Oddi dysfunction are regarded as important functional mechanisms that may promote gallstone formation. Sphincter of Oddi function disturbances may prevent normal bile flow and thus enhance the probability of common bile duct (CBD) stone formation. Previously it has been shown that there is a 7-fold increase in the prevalence of diagnosed hypothyroidism in CBD stone patients when compared with age, sex and hospital admission adjusted controls, but only a 3-fold increase in the prevalence of hypothyroidism in gallbladder (GB) stone patients. This might suggest something other than merely a bile composition-dependent mechanism.

Not unexpectedly, therefore, in both animal and human experiments thyroxine (T4) has a direct pro-relaxing effect on the sphincter of Oddi (SO) that expresses thyroid hormone receptors β1 and β2. This pro-relaxing effect of T4 is mediated through a mechanism that requires new mRNA and protein synthesis and subsequently results in the activation of ATP-dependent K+-channels. The usage of thyroxine was even suspected to dissolve gallstones.

In an animal model of rabbits in which a fatty diet induced gallstone formation, administering thyroxine was associated with a low gallstone weight, but did not dissolve the gallstones.

To our knowledge, there is only one large case control study that was appropriately adjusted for other risk factors of gallstone disease. In combination with the possible changes in the bile composition and excretion, the absence of the pro- relaxing effect of T4 might offer a possible explanation for the increased prevalence of CBD stones in hypothyroid patients, if hypothyroidism results in delayed emptying of the biliary tract. Hence if an increase in prevalence of hypothyroidism will be found associated with cholelithiasis it may have an effect on the diagnostic and therapeutic workup of the patients with gall stones

This study intends to show the prevalence of previously undiagnosed hypothyroidism in patients with gall stones.

Aim: To know the prevalence of hypothyroidism in diagnosed cases of gall stone disease.

Objectives:

1. To evaluate thyroid profile in patients with gall stone disease.
2. To show the prevalence of previously undiagnosed hypothyroidism in patients with gall stone disease.
3. To show the correlation between elevated TSH levels and symptoms of hypothyroidism in cholelithiasis patients.

MATERIALS AND METHODS

Source of Data: Both Inpatients and outpatients diagnosed to have Gallstone disease in MNR Medical College and Hospital, Sangareddy between August 2020 and November 2022.

Place of study: General surgery department, MNR Medical College and Hospital, Sangareddy.

Sample size: 102

As per hospital records, cases collected and sample size is taken as 102.

Method of Collection of Data:

Study type: Descriptive Correlative study

Inclusion criteria:

- Patients in the age group of 20-65 years diagnosed to have Gallstone disease (presence of gallstones on USG) in MNR medical college hospital
- Including prior history of cholecystectomy (past 5 years) or the presence of gallstones on ultrasound.

Exclusion criteria:

- Patients with previous history of hypothyroidism on treatment.
- Previous history of thyroid surgery or previous radioiodine exposure.
- Any patient with suspected common bile duct stone according to abdominal ultrasound.
- Pregnant females diagnosed with cholelithiasis.
- Patients who are on artificial feeding or Total Parenteral Nutrition

Method of collection of data:

A sample size of 102 consenting inpatients and outpatients in MNR Medical College Hospital diagnosed to have gallstone disease will be selected by purposive sampling technique based on inclusion and exclusion criteria. Prior to selection, they undergo routine history taking, physical examination and investigation to exclude co-existing diseases or generalized debility. Thyroid function tests will be done in these diagnosed (cholelithiasis) cases either pre- operatively or post-operatively.

Data collected includes:

- Name, Age, Sex, In Patient no (IP no), Diagnosis
- Ultrasound abdomen & pelvis.
- Thyroid function test which includes T3, T4, TSH.

Plan for data analysis:

Data collected will be analysed by Karl Pearson's Correlation Coefficient and Chi Square test.

RESULTS

In our descriptive study, 102 cases diagnosed with gallstone disease were selected by purposive sampling technique. The selected patients were investigated with thyroid function tests.

Age Distribution

Patients were between the ages of 20-65 years. Out of the 102 cases, majority of the patients were between the age of 31-40 years (35.3%), we had

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eighteen patients below 30 years (17.65%), twenty eight patients between 41-50 years (27.45%), fifteen between 51-60 years (14.7%) and five greater than 60 years of age (4.9%).

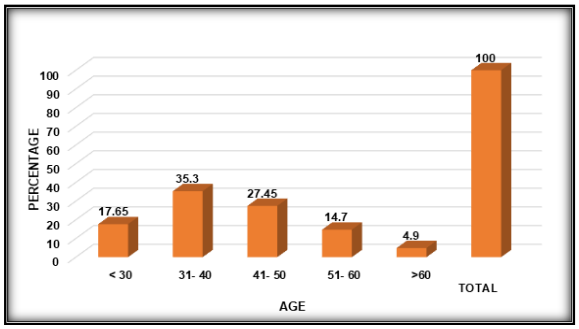

Figure 1: Age Distribution

Gender Distribution

Of the 102 patients a majority of them comprised of women (59.8%). Whereas the men were only 40.20% of the study population.

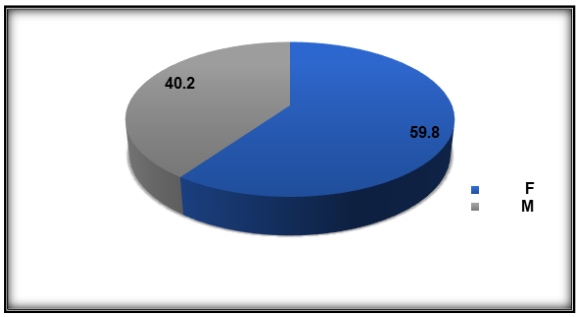

Figure 2: Gender Distribution

Clinical Presentation

67 of the 102 cases presented with pain in the right hypochondrium (65.68%). 30 cases presented with nausea, vomiting and other dyspeptic symptoms (29.41%), out of which 26 cases had tenderness in the right hypochondrium on deep palpation (25.49%). 10 patients presented with fever (9.8%). Murphy's sign was positive in 7 patients (6.86%).

Ultrasound abdomen was used as the investigation of choice to confirm the diagnosis of gallstone disease in all the 102 cases.

97 cases eventually underwent Laparoscopic cholecystectomy and 5 cases underwent Open cholecystectomy.

Histopathological examination of the specimens in the operated patients showed cholelithiasis in 93 cases (91.2%); acute calculous cholecystitis in 4 cases (3.9%); chronic calculous cholecystitis in 5 cases (4.9%).

Correlation of Thyroid Function Tests

All the patients in the study diagnosed with cholelithiasis were evaluated for thyroid function test which includes T3, T4, TSH and FT4 levels.

T3 levels

Out of 102 patients in our study, 90 patients had normal T3 levels (88.2%), 10 patients had low T3 levels (9.8%) and 2 patients had high levels (2.0%)

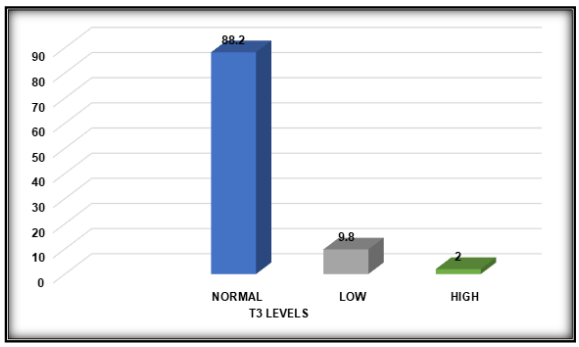

Figure 3: T3 LEVELS

T_4 Levels

Out of 102 patients, 94 patients had normal T_4 levels (92.1%), 7 patients had low T_4 levels(6.9%) and 1 patient had high T_4 levels(1.0%).

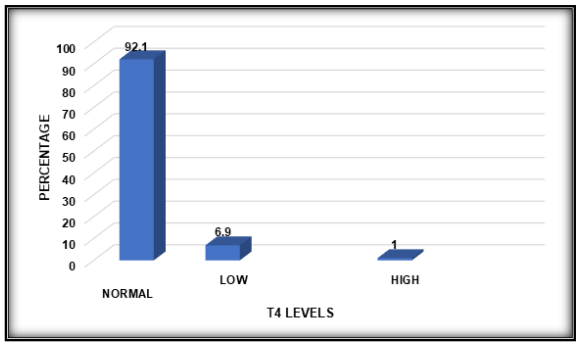

Figure 4: T4 LEVELS

TSH Levels

Out of 102 patients in our study, 16 patients had high TSH levels (15.7%), 2 patients had low TSH levels (2.0%) and 84 patients had normal TSH levels (82.3%). Out of the 16 patients with high TSH 12 patients were females and 4 patients were males.

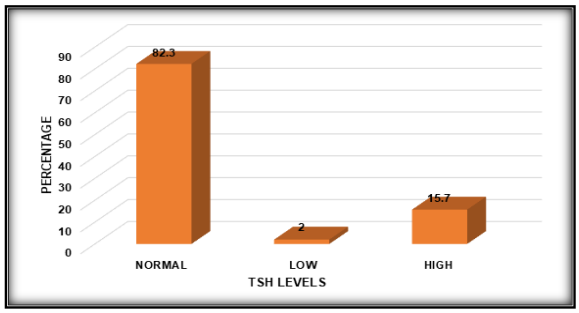

Figure 5: TSH levels

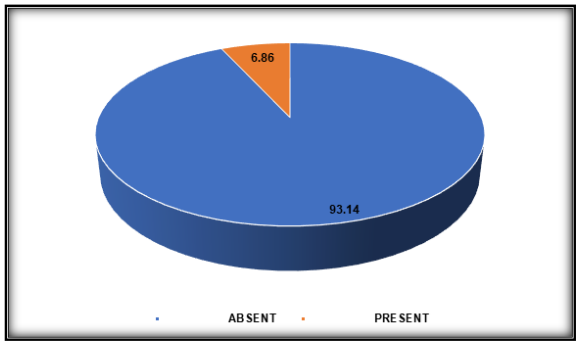

Figure 6: Symptoms Of Hypothyroidism

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Symptoms of hypothyroidism

Only 7 patients in the 102 study population had symptoms of hypothyroidism (6.86%). Also out of the 16 patients with high TSH levels, only 7 patients had symptoms of hypothyroidism.

Table 1

	Frequency	Percentage (%)
<30	18	17.65
31-40	36	35.3
41-50	28	27.45
51-60	15	14.7
>60	5	4.9
Total	102	100

Table 2

Sex	Frequency	Percentage (%)
Female	61	59.80
Male	41	40.20
Total	102	100.00

Table 3: normal reference values

	Normal reference values
T3	0.8-2 ng/ml
T4	5.1 -14.1 microgram/dl
TSH	0.27-4.2 microU/ml
FT4	0.93-1.7 ng/dl

Table 4

T3	Frequency	Percent
Normal	90	88.2
Low	10	9.8
High	2	2.0
Total	102	100.0

Table 5

T4	Frequency	Percent
Normal	94	92.1
Low	7	6.9
High	1	1.0
Total	102	100.0

Table 6

TSH	Frequency	Percent
Normal	84	82.3
Low	2	2.0
High	16	15.7
Total	102	100.0

Table 7

Symptoms of Hypothroidism	Frequency	Percent
Absent	95	93.14
Present	7	6.86
Total	102	100.0

Table 8: Correlation between T3 and symptoms of hypothyroidism in cholelithiasis

Symptoms of Hypothyroidism			
T3 Levels	**Present**	**Absent**	**Total**
Normal	4	86	90
Low	3	7	10
High	0	2	2
Total	7	95	102

Pearson correlation value: -.199

P-value: .009

Table 9: Correlation between T4 and symptoms of hypothyroidism in cholelithiasis

Symptoms of Hypothyroidism			
T4 Levels	**Present**	**Absent**	**Total**
Normal	6	88	94

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Low	1	6	7
High	0	1	1
Total	7	95	102

Pearson Correlation Value: .047
P- Value: .701

Table 10: Correlation between TSH and symptoms of hypothyroidism in cholelithiasis

Symptoms of Hypothyroidism			
TSH	**Present**	**Absent**	**Total**
Normal	0	84	84
Low	0	2	2
High	7	9	16
Total	7	95	102

Pearson correlation value: -.618
p- value: .000

Table 11: Correlation between thyroid profile and symptoms of hypothyroidism

	T3	**T4**	**TSH**
Pearson Correlation	-.199	-.047	-.618
p=(significant if p <0.05)	.009	.701	.000
n	102	102	102

(p= p value as calculated by chi-square test N: sample size)

Correlation between high serum TSH, Low T3 & T4 levels and presence of symptoms of HYPOTHYROIDISM in CHOLELITHIASIS was done. Negative correlation was observed between thyroid profile and presence of symptoms of hypothyroidism. High serum TSH was highly significant, lowT3 level weakly significant with presence of symptoms of hypothyroidism in our study.

DISCUSSION

Earlier, an association between gallstone and diagnosed hypothyroidism and delayed emptying of the biliary tract in experimental and clinical hypothyroidism have been shown, explained at least partly by the lack of pro-relaxing effect of T4 on the sphincter of Oddi contractility.

In this study we further investigated the prevalence of previously undiagnosed hypothyroid abnormalities in gallstone patients. The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting early thyroid failure is an increased TSH concentration. In the subclinical form, an increased TSH level is accompanied by a normal T4 and T3 level, and the patient is asymptomatic.

In this study, the higher proportion of hypothyroidism in women with cholelithiasis compared to men was probably due to the earlier symptomatology of gallstone disease in women as well as the higher incidence of thyroid disease in women in general. This leads to an earlier detection and treatment of hypothyroidism in women.

A study conducted by Rana Ranjit Singh in 2016 demonstrated the percentage of males with gallstone disease diagnosed as hypothyroid, euthyroid and hyperthyroid is 24%, 64% and12% respectively. The percentage of females with gallstones diagnosed hypothyroid, euthyroid and hyperthyroid was 24.4%, 65.85 and 1% respectively.[13]

In a study conducted in August 2016 Aishwin Saravana kumar in Coimbatore (Tamil Nadu), out of 50 patients 34% were male and 66% were female. In the study 66% were euthyroid, 14% were sub clinical hypothyroid, 10% hypothyroid and 10% hyperthyroid. Of the 14% subclinical hypothyroid, 4% were in the age group 30-45, 10% were in the age group of more than 45. Hypothyroidism was more in female patients (80%).[14]

In a study conducted by Mir Mujtaba Ahmad in 2015 at SMHS Srinagar over a period of 2 years on a total of 100 patients, 50 diagnosed as having cholelithiasis and 50 having choledocholithiasis. A complete history, detailed clinical examination followed by evaluation as per protocol was done. There was an increased prevalence of choledocholithiasis with increasing age (maximum patients in age group 51-60) with female predominance in patients diagnosed as choledocholithiasis, thereby implying increasing age and female gender as risk factors for choledocholithiasis.[15,16]

There was a prevalence of hypothyroidism in 8% of cholelithiasis group with subclinical hypothyroidism present in maximum number of patients (75%) and clinical in 25% of patients. Abnormal high levels of serum TSH and cholesterol were reported in 12 cases (8%) and in 15 cases (10%) respectively.[17]

A cross sectional study was done in MCH Trivandrum in 2015 to know the prevalence of subclinical hypothyroidism in patients with symptomatic gall stone disease. During which period total of 93 patients with gall stone disease were studied to see the relation between hypothyroidism and gall stones. Out of 92 patients with gallstone 50 (54.3%) were females and 42 (45.7%) were males. Thyroid disorder in form of subclinical hypothyroidism was found in 12 (13%), from this 10 (83.3%) were females and males were 2 (16.7%). From 92 cases with gallstones diseases 7(7.6%) cases complaining from goiter. Peak age was less than 40

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years. In this study, the higher proportion of hypothyroidism in women with cholelithiasis compared to men was mainly due the earlier symptomatology of gallstone disease in women as well as the higher incidence of thyroid disease in women in general.[15]

A study was conducted by P Sundeshwari et al in 2014 at GRH Madurai on 200 gallstone patients. Among them, 18 patients had subclinical hypothyroidism and 6 patients had clinical hypothyroidism. A total of 12% of gallstone patients were diagnosed to have hypothyroidism showing that there is association of hypothyroidism with gallstone disease.[16]

A study conducted by Suaad L Ibrahim in 2014 to measure level of TSH in serum blood of (100) patients with gallstones diagnosed by sonographically or current cholecystectomy with regard to the differences between sex of patients and predominated of gallstone type with age. In this study, there were 10 (0.1%), 38(38%), and 52(52%) patients for low, normal and high levels of TSH respectively. It showed a high proportion of females (53%) compared to the males (47%). Females were demonstrated high prevalence of normal TSH (71.69%), 13.20% and 15 for both high and low levels TSH respectively. while males demonstrated high prevalence (95.47%) of high levels of TSH and (4.53%) of low levels of TSH.[18]

A cross sectional study was done in Al-Sader Teaching Hospital in Al Najaf city between 15th of February 2008 and 1st of November 2009 of 225 cases were taken to show relation between gallstone and hypothyroidism. Out of 225 patients with gallstone 198 (88%) were females and 27 (12%) males. Thyroid disorder in form of hypothyroidism was found in 24 (10.6%), from this percentage 22 (9.7%) were females and from this 18 (8.0%) were subclinical and 4 (1.7%) were clinical hypothyroidism and males were 2 (0.9%) with subclinical cases. Out of 225 cases with gallstones, 22(9.7%) cases complaining from goiter with peak age between 51- 60 years.[19]

In a study done by Johanna L, Gediminas K (2007), the prevalence of subclinical hypothyroidism was 11.4% in gallstones and none of the patients was clinically hypothyroid.[20]

In a study Hassan H Zaini et al in 2008 on 225 patients, 24 were of hypothyroid. Out of these in laboratory investigation we found that 20 cases recorded with high TSH and low T3, T4, 3 cases with high TSH and low T4 and 1 case with high TSH and low T3. These results are comparable to our study where out of 200 cases 27 have low FT4 23 and 25 have low FT3.[19]

Furthermore, a study by Laukarrien et al,[7] found a prevalence of subclinical hypothyroidism 10.2% which is slightly high as compared to present study that showing the prevalence of subclinical hypothyroidism among cholelithiasis patients found (7.8%) this may be due to the fact that their study done in endemic areas of iodine deficiency. The present study shows an increase prevalence of subclinical hypothyroidism with increasing age of patients and this was maximum at age above 40 years (7/8), younger than this age the prevalence shown to be less (1/8) of patients.[20]

On the other hand, a study conducted by Volzke H et al,[21] thyroid function and gallstones shows that women were affected nearly twice as often as men, while gallstones were only slightly more often detected by ultrasound in women than in men.

Volzke H et al,[21] earlier diagnosis and treatment of hypothyroidism in women compared to men. This assumption is supported by the fact that the association between high serum TSH levels and cholelithiasis was mainly found in females with sonographically detected gallstones as proved in our study and still more predominant in female gender. So, patients with gall stone who are female gender, ≥ 40 years, positive family history, and with single stone as found by abdominal ultrasound should be re-evaluated and assessed by detailed history taking, thorough clinical examination and laboratory confirmation to identify possible subclinical hypothyroid state.

CONCLUSION

Several recent studies report an association between hypothyroidism or subclinical hypothyroidism and gallstones. Recent studies have demonstrated low bile flow in hypothyroid subjects. Furthermore the sphincter of Oddi expresses thyroid hormone receptors and thyroxine has a direct pro-relaxing effect on the sphincters. Both low bile flow and sphincter of Oddi dysfunction are regarded as an important reason that may promote gall stone formation From our descriptive study of 102 gallstone disease patients done in MNR Medical College Hospital, Sangareddy, we hereby conclude that

- Gallstone disease was more common in the 31-50 year age group and was more commonly seen in females than males.
- -Out of 102 patients, 84 patients (82.3%) had normal TSH, 16 patients (15.7%) had increased TSH of which 6.86% of the patients had symptoms of hypothyroidism(undiagnosed).
- Strong negative correlation was observed between high serum TSH levels and presence of symptoms of hypothyroidism which was significant.

Hence the possibility of hypothyroidism can be suspected in a patient with gall stone disease especially in females between third to fifth decade age group and all the patients with gall stone disease should be screened for presence of hypothyroidism.

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