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Correlation of Subclinical Hypothyroidism in Cholelithiasis in and around Coimbatore

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I. Introduction

Gall stones are the most common biliary pathology which may be of three main types:cholesterol,pigments or mixed.In Asia 80% are pigment stones, rest being cholesterol or mixed stones. Mixed stones contain cholesterol admixture of calcium salts,bile acids,bile pigments and phospholipids.

Cholesterol stones arise due to a disorder of the physio-chemical equilibirium which normally maintains the cholesterol in miscellar form in the bile.The pathogenesis of gall stones is a complete process involving factors affecting bile content and bile flow.

Recent studies concentrate on gall stones and thyroid hormones –T3 and T4 have effect on both bile content and bile flow.Patients with hypothyroidism have serum level of cholesterol approximately50% higher level than in euthyroid patients and 90%of all hypothyroid patients have elevated cholesterol level.Likewise low levels of T4 have an effect in relaxing the sphincter of oddi,leading to biliary stasis and stone formation.

II. Review Of Literature

The prevalence of cholelithiasis has been reported as approximately 5%-26% in different countries.The pathogenesis of cholelithiasis is not unique, but appears to be multifactorial.It has been shown that disturbances in lipid metabolism that occur during hypothyroidism, particularly cholesterol pathway, changes the rate of bile excretion and lead to the formation of gall stones.Recently, the pro-relaxing effect of serum total thyroxin (T4) on both human and pig sphincter of Oddi (SO) has been proved.Possibly, the lack of T4 may contribute to SO contractility which in turn not only disturbs the normal bile flow but also prohibits the passage of stones formed in the gallbladder to the duodenum. Some researchers have reported a higher prevalence of both hypothyroidism and subclinical hypothyroidism in cholelithiasis which supports a possible relation between low T4 levels and gall stones.

To our knowledge there are only few published articles that have discussed the prevalence of undiagnosed subclinical hypothyroidism among gall stones patients. The current study investigates the prevalence of subclinical hypothyroidism in patients with gall stones.

During last two decades the etiologies of cholelithiasis have been evaluated more seriously. In addition to classic risk factors such as age, gender, obesity and genetics, the associations between gall stones and delayed emptying of the biliary tract in hypothyroidism have been shown. This is related to lack of the prorelaxing effect of the thyroid hormone on SO contractility.In this study we have evaluated the prevalence of thyroid dysfunction in patients with gall stones.

Serum TSH is a hallmark of thyroid dysfunction. The subclinical form of hypothyroidism is characterized by increased serum TSH levels along with normal serum T4 levels and a lack of clinical symptoms.

Normal Value Of TSH Is 0.4-4.2 miu/ml. To say as Subclinical Hypothyroidism,TSH should be more than 4.2mIU/ml.

It has been classically divided into:
Mildly Elevated:4.5-10mIU/ml
Marketedly Elevated:>10mIU/ml

Pathogenesis of Gall Stones in Hypothyroidism:
Lack of thyroxin leads to:

1 . Decreased Liver Cholesterol Metabolism

Bile Cholesterol Hyper saturation

Impairs Motility, Contractility And Filling of Gall Bladder

Retention of Cholesterol Crystals, Nucleation and Growth of Gall Stones.

2. Diminishes Bile Secretion from Hepatocytes

Impaired Clearance of Precipitates from CBD

3. Reduces Sphincter of Relaxation

Resulting In Delayed Bile Flow

Formation and Accumulation of CBD Stones

As the 3 most probable causes for gall stone formation are related to hypothyroidism,it is shown clearly that there is correlation between gall stones and thyroid dysfunction.

The initial formation of bile cholesterol crystals may begin during the untreated period of hypothyroidism and stones may continue to develop even after the thyroxine replacement has begun. Studies with subclinical hypothyroid patients have demonstrated a positive effect in the changes in the serum cholesterol level by early replacement with thyroxine.

In conclusion,disturbances in lipid metabolism which occur during hypothyroidism lead to the formation of gallstones. This study aims to evaluate the thyroid function pattern in patients with gall stones.Gall stones have its own surgical related morbidity and mortality and comorbid states like cardiovascular problems, acute MI, acute stroke. If serum TSH is used as a marker or screening test for cholelithiasis, all these morbid and comorbid states can be avoided.

III. Aims And Objectives

- To check thyroid hormone levels TSH, T3 and T4 in patients who have undergone cholecystectomy in and around Coimbatore.
- To check thyroid status in patients (sample size-50) who have undergone cholecystectomy in and around Coimbatore,there by dividing into euthyroid,hypothyroid,hyperthyroid and subclinically hypothyroid,correlating the prevelance of subclinical hypothyroidism in patients with cholelithiasis,there by recommending serum TSH as a serum marker for cholelithiasis.

IV. Materials And Methods

Type of study: retrospective observational study
Study Design: 50 patients who have undergone cholecystectomy for cholelithiasis are selected
based upon the selection criteria given below and subjected to thyroid function tests by collecting blood samples after 12 hours of fasting and send to lab within 1 hour for estimation.
Study Population: both men and women who have undergone cholecystectomy during the period of given 2 months.
Sample Size: 50
Selection Criteria:
Inclusion Criteria: both male and female undergone cholecystectomy for cholelithiasis

Exclusion Criteria:

Excluded were patients with a history of previously diagnosed or treated thyroid function abnormalities, history of thyroidectomy, pregnancy, serious underlying diseases, sepsis or cholanlangitis and those prescribed medications known to affect the thyroid function test such as
phenytoin, carbamazepin, metoclopramide, amiodarone, and lithium.

Data collection procedure: 3-4 ml of venous blood is collected and sent to the laboratory for estimation of serum T3 T4 AND TSH.

Instruments Used: centaur using CLIA method

Confidentiality: The details of the participants and their blood values will not be revealed to anybody else other than the concerned participant.

Plan of analysis: Correlation of increased TSH in patients with cholelithiasis

Ethical Considerations: Institutional Ethical committee clearance will be obtained and Consent form will be obtained from each participant.

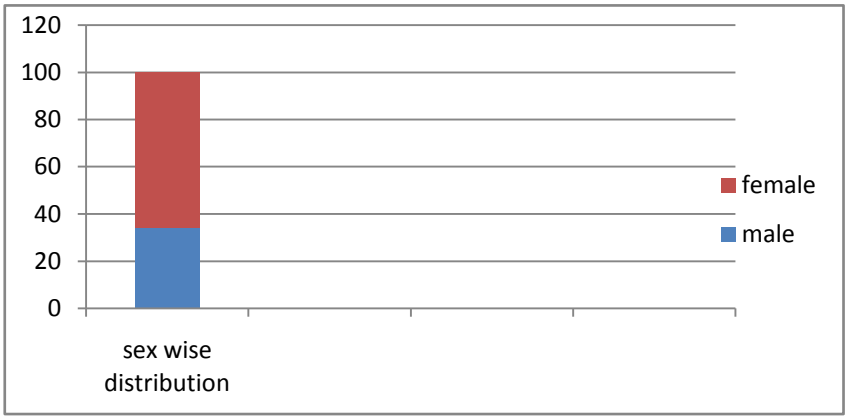
Observation and Results

1. Sex Wise Distribution:

MALE	FEMALE
17(34%)	33(66%)

It is observed from the above recordings that Gall stones are more common in women(66%), than in men(34%). This is because earlier symptomatology of gall stone disease in women as well as higher incidence of thyroid disease in women. This is because earlier symptomatology of gall stone disease in women as well as higher incidence of thyroid disease in women.

1.Sex Wise Distribution

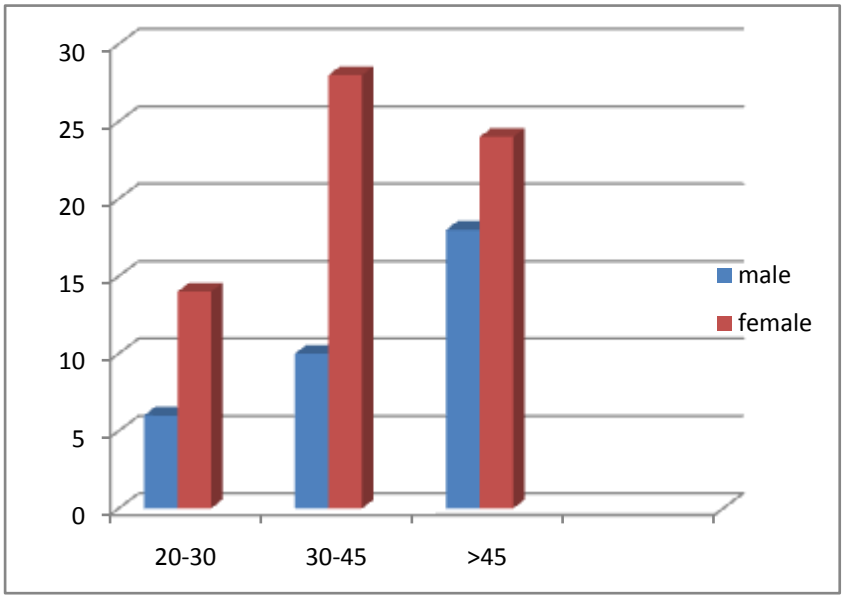


2. Age Wise Distribution:

AGE	MALE	FEMALE	TOTAL
20-30	3 (6%)	7 (14%)	10(20%)
30-45	5 (10%)	14 (28%)	19(38%)
>45	9 (18 %)	12 (24%)	21(42%)

It is observed from the above readings,that of the patients who have undergone cholecystectomy, 20% were in the age group of 20-30, and 38% were in the age group of 30-45, and 42% were in the age group of more than 45.It has creeped slowly from the age group of 30-45, reaches peak in the age group of more than 45. This reading also tells that it is more common in females that too more common in the age group of >45 where the sexual hormones are in an imbalanced state.

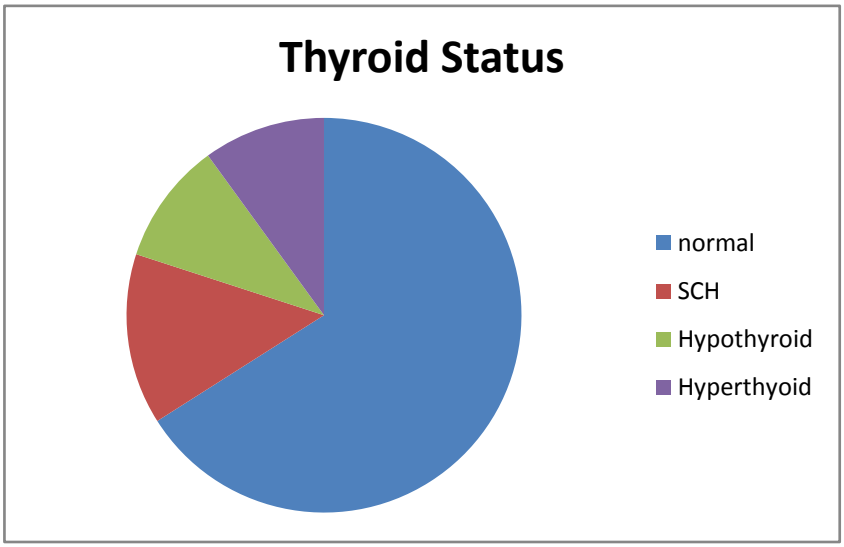
2. Age Wise Distribution:



3. Thyroid Status

	NO OF PATIENTS	PERCENTAGE
NORMAL	33	66%
SCH	7	14%
HYPOTHYROID	5	10%
HYPERTHYROID	5	10%

Of the 50 patients undergone cholecystectomy, 33 (66%) were normothyroid. 5 patients (10%) are hypothyroid,

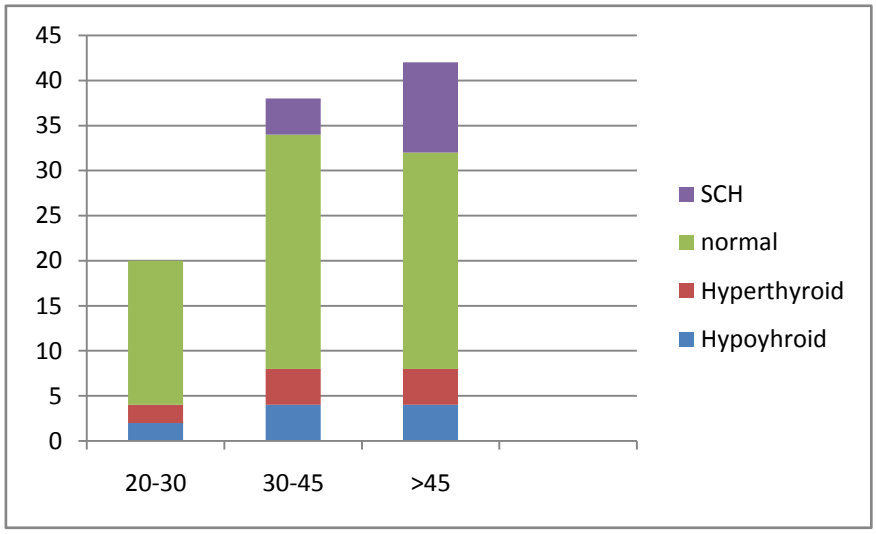


5(10%) are hyperthyroid, 7 (14%) were sub clinically hypothyroid.

4.Prevelance of hypo/ hyper/ normothyroid / SCH age wise.

Age	Hypothyroid	%	Hyperthyroid	%	Normothyroid	%	SCH	%
20-30	1	2	1	2	8	16	-	-
30-45	2	4	2	4	13	26	2	4
>45	2	4	2	4	12	24	5	10

Of the 14% of SCH, 4 % are in the age group of 30-45, 10% are in the age group of more than 45.



5. Sexwise Distribution Of Hypothyroid Patients:

MALE	FEMALE
1(20%)	4(80%)

Hypothyroidism more common in female (80%).

6. Sexwise distribution of subclinical hypothyroidism :

MALE	FEMALE
3(43%)	4(57%)

7.Agewise distribution of subclinical hypothyroidism :

AGE	MALE	FEMALE
20-30	NIL	NIL
30-45	1(33.3%)	1(25%)
>45	2(66.6%)	3(75%)

Of the SCH females 75% are in the group >45 and SCH males only 66.6%are in the age group >45, which tells SCH more common in females that too more common in age group >45.

V. Discussion

1. Earlier an association between gall stone and hypothyroidism is well known explained atleast partly by the lack of prorelaxing effect of T4 on the sphincter of oddi contractility.

2. In the study we further investigated the prevelance of Subclinical hypothyroidism in gall stone patients. The laboratory hallmark of primary hypothyroidism and the most sensitive test for detecting thyroid failure is an increased TSH concentration.

3. In the Subclinical form, an increased TSH is accompanied by a normal T4 and T3 level and the patient is asymptomatic.

4. As everyone knows the three F's associated with gall stones are Forty, Fatty and Female. This study also supports the above said saying by giving a recording of 66% of gall stones in women compared to 34% in men.

5.In this study majority of patients are in the age group of >45(42%) and this is contributed to the sex hormone imbalance of this age group which is similar to the study done by JOHANNA L,GEDIMINAS K(2007).In a study done by JOHANNA L,GEDIMINAS K(2007),the incidence of subclinical hypothyroidism was 11.4% ,which is close to that of this study (14%).The prevelance of hypothyroidism was nil in that study, but in this study prevelance of hypothyroidism is 10%.

VI. Conclusion

1. The prevelance of Subclinical hypothyroidism in gall stones was the same as other studies (11% Vs 14%).
2.Among SCH,the incidence is more common in the age group of >45.So we recommend that TSH level should be checked for every patient with cholelithiasis and it may be a SERUM MARKER for detecting SCH and treat it,before it emerges as a full blown hypothyroidism and its co-morbid states due to hypercholesterolemia like CVA and CVD.

Summary

Subclinical hypothyroidism is a thyroid dysfunction with elevated serum TSH and normal T3 and T4 levels.Thyroid hormones influence the cholesterol metabolism and also have a prorelaxing effect in the sphincter of oddi.Whenever the thyroid function is disturbed-decreased T3 T4 levels will lead to gall stone formation.From the above study,it is evident that subclinical hypothyroidism is also associated with gall stones and that too in women ,in the age group of more than 45.Since it is associated with increased serum TSH alone ,this can be used as a serum marker and further complications of gall stones can be avoided.

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