Original Research Article

A case control study to assess the association between thyroid function and the risk of cholelithiasis

Abhiranjan Prasad[1*], K.K.Sinha[2]

[1]Senior Resident, Department of General Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India

[2]Associate Professor, Department of General Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India

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Abstract

Aim: The aim of our study is to analyze the association between thyroid function and the risk of cholelithiasis. **Material and methods:** The case control study was conducted Department of General Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for one year. This study was a hospital based case control study where two groups were formed, patients diagnosed as gall stone disease and subjected to elective cholecystectomies (cases) and patients admitted for other diseases (control). Subsequent evaluation was done with emphasis on thyroid profile and lipid profile. Detailed history of the patients, Complete clinical examination, Complete blood count, KFT, Na^+/K^+, Blood sugars, LFT Chest radiograph, ECG,Trans abdominal USG, Thyroid profile (T3,T4,FT4,TSH) and Stone analysis were evaluated. Results: Majority of the cases were in the 40-50 year age group (35%) whereas controls were in the 30-40 year age group (34%). The mean age was 43.25 in cases and 45.5 in controls. P value = 0.412 (Insignificant). Maximum number of patients who became a part of this study were from rural areas, thus reflecting the pattern of patients attending our hospital. The number of patients from rural areas was 138 (69%) and those from urban areas were 62 (31%). P value=0.041 (Significant). In our study there was a prevalence of 40% of hypothyroidism in cases as compared to 24% in the controls, showing an increased prevalence in the cases as compared to the control group. This difference was statistically significant. None of our subjects were hyperthyroid. In our study among the cholelithiasis patients (cases) the prevalence of subclinical hypothyroidism was 31% and that of overt hypothyroidism was 9% respectively whereas in controls the prevalence of subclinical hypothyroidism was 18% and overt hypothyroidism was 6%. The majority of the hypothyroid patients in the cases group (cholelithiasis) were between 40 to 50 years. The males affected with hypothyroidism was (22.5%) as compared to females (77.5%) which shows higher prevalence among females in our population. **Conclusion:** Hypothyroidism was more common in the gallstone patients compared with controls. Prevalence of hypothyroidism in gallstone patients was more common in females compared to males.

Keywords: Gall Stones, Hypothyroidism, TSH.

Introduction

Cholelithiasis is a prevalent abdominal disorder resulting in hospital admissions in Western countries. The prevalence of cholelithiasis has been reported as approximately 5%-26% in different countries[1]. The prevalence of cholelithiasis in Iran is approximately 5%, however one survey on the prevalence of cholelithiasis in Iranian cadavers has been reported it at 6.3%[2]. The pathogenesis of cholelithiasis is not unique, but appears to be multifactorial[1,3].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 proven[4,5]. 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 common bile duct (CBD) stones which supports a possible relation between low T4 levels and CBD stones[5,6]. Bile stasis, bactibilia, chemical imbalances, pH imbalances, change of bile composition and formation of sludge are among the principle factors thought to lead to formation of gallstones. Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India too is no exception. 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. In the present study, we have tried to determine an association between gall stone disease, and previously diagnosed and undiagnosed hypothyroidism in patients presenting to our hospital for treatment. Previous studies[7,8] that investigated the association between thyroid function and gallstone disease in human beings, were conducted in a series of patients with potential for selection bias that may have produced false positive results. Furthermore, the statistical analyses were only controlled for age, but not for further confounders in both studies[7,8]. To our knowledge, there is only one large casecontrol study[9] that was appropriately adjusted for other risk factors of gallstone disease. In this study[9], no independent relation between thyroid disorders and gallstone formation was found. Unfortunately, the exposure was only defined as previous history of thyroid disease, and assessments of the current thyroid function status were not included. Moreover, there are currently no investigations that also include ultrasound to evaluate asymptomatic gallstones in this context. Therefore, the aim of our study is to

**Correspondence*
Dr. Abhiranjan Prasad
Senior Resident, Department of General Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.
E-mail: abhiranjan04g@gmail.com

analyze the association between thyroid function and the risk of cholelithiasis .

Material and methods

The case control study was conducted Department of General Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for one year.

Methodology

This study was a hospital based case control study where two groups were formed, patients diagnosed as gall stone disease and subjected to elective cholecystectomies (cases) and patients admitted for other diseases (control). Subsequent evaluation was done with emphasis on thyroid profile and lipid profile. Detailed history of the patients ,Complete clinical examination, Complete blood count, KFT, Na^+/K^+, Blood sugars, LFT Chest radiograph, ECG,Trans abdominal USG,Thyroid profile (T3,T4,FT4,TSH) and Stone analysis were evaluated.

Patients diagnosed with gall stone disease (cholelithiasis) were included and were subjected to elective cholecystectomy were include as a case and Patients with no history of cholelithiasis, liver diseases such as elevation of serum bilirubin or liver enzymes and admitted for diseases other than those affected by thyroid dysfunction were include in control group.

Patients with a history of Previous cholecystectomy, Thyroidectomy, Pregnancy, Oral contraceptives, Liver or renal failure and those prescribed medications known to affect the thyroid function test such as phenytoin, carbamazepine, metoclopramide, amiodarone and lithium were exclude from this study.

Results

In our study there was a female predominance with a total of 157 (78.5%) females and 43 (21.5%) males. In the cases there was a distribution of 82% females and 18% males in the cholelithiasis group showing a 4:1 Female to Male ratio. Majority of the cases were in the 40-50 year age group (35%) whereas controls were in the 30-40 year age group (34%). The mean age was 43.25 in cases and 45.5 in controls. P value = 0.412 (Insignificant). Maximum number of patients who became a part of this study were from rural areas, thus reflecting the pattern of patients attending our hospital. The number of patients from rural areas was 138 (69%) and those from urban areas were 62 (31%). P value = 0.041 (Significant).(Table 1)

Table 1:Demographic Profile of Patients

Sex	Cases	Controls
Males	18(18%)	25 (25%)
Females	82(82%)	75(75%)
Age Group		
Below 20 years	3 (3%)	1 (1%)
20-30	20 (20%)	18 (18%)
30-40	24 (24%)	34 (34%)
40-50	35(35%)	27 (30%)
50-60	13 (15)	12 (17%)
Above 60	5(5)	8 (8%)
Region		
Rural	63(63%)	75 (75%)
Urban	37 (37 %)	25 (25%)

A significant number of patients in the cases group (40%) were hypothyroid compared to the control group (24%) and the difference was statistically significant. None among our subjects was hyperthyroid. P value= <0.001 (significant).(Table.2)

Table 2:Thyroid Status of the patients

Thyroid Status	Cases (n=100)	Control (n=100)
Hypothyroid(TSH↑)	40(40%)	24 (24%)
Euthyroid(TSH=Normal)	60 (60%)	76 (76%)
Hyperthyroid(TSH↓)	0 (0%)	0(0%)
TFT		
Subclinical Hypothyroidism↑TSH+Normal FT4	31 (31%)	18 (18%)
Overt Hypothyroidism↑TSH+FT4↓	9(9%)	6 (6%)

The total prevalence of subclinical hypothyroidism in our study was observed as 31% in cases as compared to 18% in controls showing a significant increased prevalence in the cholelithiasis (cases) group. (table.2)The majority of the hypothyroid patients in the cases group (cholelithiasis) were between 40 to 50 years.

Table 3:Hypothyroid patients in the cases group and control group

Age	Hypothyroid patients in cases =40	Hypothyroid in control =24
Below 20	0	0
20 - 30	4	5
30 - 40	11	7
40 - 50	14	3
50- 60	5	3
Above 60	6	6

Table 4:Sex distribution of hypothyroidism in cholelithiasis

Sex	Hypothyroid=40	Euthyroid=60
Males	9 (22.5%)	9 (15%)
Females	31 (77.5%)	51 (85%)

The males affected with hypothyroidism was (22.5%) as compared to females (77.5%) which shows higher prevalence among females in our population.(table 4) Among the cholelithiasis group majority number of patients had cholesterol stones 77% and 19% of patients had mixed stones. (Table 5)

Table 5: Stone Analysis

Type of Stones	Number of cases (N=100)
Cholesterol	77 (77%)
Mixed	19 (19%)
Pigment	4 (4%)

The percentage of formation of cholesterol stones was higher in the hypothyroid patients (92.5%) as compared to euthyroid patients (68.33%) with a significant result. P value<0.005(significant).

Table 6: Stone analysis between hypothyroid and euthyroid patients

Type of stone	Hypothyroid=40	Euthyroid=60
Cholesterol	37 (92.5%)	41 (68.33%)
Mixed	3 (7.5%)	14 (25.0%)
Pigment	0 (0%)	5 (5.4%)

Discussion

Gallstones are one of the commonest surgical problems encountered with an incidence ranging from 5-30%. The incidence increases with age and in female gender the predisposition to gallstone formation is more with increasing age, parity, dyslipidemia and hypothyroidism etc.The possible relation between cholelithiasis and hypothyroidism has been an area of interest for researchers all over the world and it needs further research to draw any conclusion and to establish facts.

In our study the age group of patients in both the study and the control group was 12-77 yrs with Majority of the cases were in the 40-50 year age group (35%) whereas controls were in the 30-40 year age group (34%). The mean age was 43.25 in cases and 45.5 in controls. P value = 0.412. The age group was similarly distributed in both groups. There was no statistical difference in age group between two groups. Nakeebet al[10]in their study found that the subjects with a history of symptomatic gallstones were significantly older than those subjects with no history of gallstones (58.2±10.1 vs. 50.9±14.0 years, *P*<.001) whereas in our study the average age group was younger. Our finding is consistent with the study of Evehartet al[11]who had similar results and has reported that the female to male ratio of gallstone and gallbladder disease approaches 4:1 in younger subjects (<40 years of age). The female to male ratio decreases to 2:1 in older age groups. Both the prevalence and incidence of gallstone diseases increases with age.

In our study there was a female predominance with a total of 157 (78.5%) females and 43 (21.5%) males. In the cases there was a distribution of 82% females and 18% males in the cholelithiasis group showing a 4:1 Female to Male ratio. Schirmer et al [12]also had similar results in the gender pattern among cholelithiasis patients and has reported that cholelithiasis is more common in females then males, with female to male ratio about 4:1, while the incidence becomes equal in both gender in older age. This may be because of the basic hormonal differences between males and females, together with the differences that might exist due to co-expression of sex hormone receptors in the gallbladder of both sexes. Maximum number of patients who became a part of this study were from rural areas, thus reflecting the pattern of patients attending our hospital. The number of patients from rural areas was 138 (69%) and those from urban areas were 62 (31%).

In our study there was a prevalence of 40% of hypothyroidism in cases as compared to 24% in the controls, showing an increased prevalence in the cases as compared to the control group. This difference was statistically significant. None of our subjects were hyperthyroid. In our study among the cholelithiasis patients (cases) the prevalence of subclinical hypothyroidism was 31% and that of overt hypothyroidism was 9% respectively whereas in controls the prevalence of subclinical hypothyroidism was 18% and overt hypothyroidism was 6%. Bashir H et al[13]in their study found a prevalence of subclinical hypothyroidism as 21.3% and overt hypothyroidism 9.0% with a total percentage of hypothyroid patients 30.6% in Kashmir. The results from our study are almost similar to this study but show an increased prevalence among the cholelithiasis group as compared to controls. Ajdarkosh et al[14] had similar results in his study of thyroid status among choledocholithiasis. Subclinical hypothyroidism was noted in 30.6% of cases and 22.5% of controls. Overt hypothyroidism was observed as 11.3% in cases and 10.8% in controls. Laukkarinen J et al[15] in their study found a prevalence of hypothyroidism in 10.2% in choledocholithiasis group as compared to 2.8% in the control group and in the same study found a prevalence of 23% subclinical hypothyroidism in females more than 60 years of age. These results were almost similar to our study. Laukkarinen J et al [16] in another study concluded that hypothyroidism is common in bile duct stones, thus supporting our findings with cholelithiasis. However the increased prevalence of hypothyroidism (both subclinical and clinical hypothyroidism) in cases as compared to controls clearly demonstrate that hypothyroidism plays a role in gallstone formation.

In this study, the higher proportion of hypothyroidism in women with cholelithiasis compared to men was mainly due to the earlier symptomatology of gallstone disease in women as well as the higher incidence of thyroid disease in women in general. The majority of the patients having hypothyroidism were in the age group 40-50 years, 78.5% females and 21.5% males. Laukkarinen J et al[15] in their study found similar results and concluded that with increasing age there was increased prevalence of hypothyroidism with maximum number of patients in the age group of around 60 years predominantly females. The findings are consistent with our study. Bashir H et al[13] had similar results in their study and observed prevalence of

hypothyroidism more in females 81.8% as compared to males 18.2%.

Majority of the patients had cholesterol stones 77% with prevalence of mixed stones as 19% and pigment stones 4% respectively. Stone analysis varies in different studies all over the world depending upon dietary pattern, ethnicity, and regional variation. June S et al[17] in a study observed the pattern of type of gall stone distribution in USA was 88% cholesterol stones whereas Whiting J et al[18] observed a prevalence of 91% cholesterol stones in Australia. Study conducted by Sarin et al[19] RK Tandon et al[20]concluded that around eighty percent of gallstones in northern India are cholesterol stones, similar study done in Kashmir by Hussain A et al[21] also had results that were similar to our study and showed maximum percentage of cholesterol gall stones in this region.

In our study among the hypothyroid patients the prevalence of cholesterol stones was 92.5% as compared to 68.33% in euthyroid patients. Thus, showing a positive association between hypothyroidism and cholesterol stones was observed in our study. Similar results were observed by Hassan H et al [22] in their study where they observed cholesterol stones more prevalent in high TSH group as compared to mixed and pigment stones, also the serum cholesterol levels were higher in cholesterol type gallstone. However it further needs an elaborate and a larger epidemiological study and research to find out the prevalent gallstone type in hypothyroid patients

Conclusion

Hypothyroidism was more common in the gallstone patients compared with controls. Prevalence of hypothyroidism in gallstone patients was more common in females compared to males.

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