

## Prevalence of hypothyroidism in patients with cholelithiasis: A cross sectional study

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### Abstract

**Introduction:** Cholelithiasis is a common pathology of the gall bladder affecting about 10 to 15% of the adults. More than 80% of the patients with cholelithiasis are asymptomatic. Hypothyroidism is one of the endocrine disorders and is believed to cause gall stone formation due to the hyperlipidemia, motility disorders affecting the bile duct and sphincter of Oddi. The aim of our study is to determine the prevalence of hypothyroidism in patients with cholelithiasis admitted in tertiary care hospital.

**Material and Methods:** This was a descriptive cross sectional study conducted at Department of Surgery, Mardan Medical Complex and Mardan Teaching Institutions, Mardan, Pakistan from May 2018 to April 2019 for duration of one year. The sample size was 174 and consecutive non-probability sampling technique was used for the sampling. All the patients presenting with cholelithiasis diagnosed on the basis of ultrasonography, with age 20 to 70 years, included in the study. All the data like age, gender, height weight, BMI, hypothyroidism were recorded in a pre-designed proforma. All the data was analyzed in SPSS version 20. Mean and standard deviation was calculated for numerical variables and frequencies and percentages were calculated for qualitative variables. Chi square test for categorical variables was applied with p-value of < 0.05 as significant.

**Results:** The mean and standard deviation of age, height, weight and BMI were  $41.66 \pm 13$ ,  $165.15 \pm 11.35$ ,  $68.17 \pm 11.95$  and  $25.69 \pm 7.19$  respectively. Out of 174-patients with cholelithiasis, 47.1% patients were from the age group 41-50 years. 14.4% patients were hypothyroid pre-dominantly females. Among 97-female patients 20 (20.6%) were hypothyroid and among 77-male patients 5 (6.5%) were hypothyroid. Hypothyroidism in male and female was statistically significant.

**Conclusions:** This study was conducted to determine the relationship between hypothyroidism and cholelithiasis. It was concluded that hypothyroidism was more common in female, obese and elder patients. The gender distribution of the hypothyroidism in patients with cholelithiasis was statistically significant while all other variables were statistically not significant.

**Keywords:** Hypothyroidism, cholelithiasis, hyperlipidemia, motility disorders affecting the bile duct and sphincter of Oddi

### Introduction:

Cholelithiasis is a common pathology of the gall bladder affecting about 10 to 15% of the adults.<sup>1</sup> More than 80% of the patients with cholelithiasis are asymptomatic.<sup>2</sup> The prevalence of cholelithiasis depends upon age, gender, ethnicity and other co morbidities. The presence of

stones in the gall bladder is more common in female as compared to male.<sup>3</sup> It is believed that estrogen plays important role in the formation of gall stone due to its effects on cholesterol. Gall stones are less common in children and are considered as disease of elder people.<sup>4</sup> Children with hemolytic anemia are affected more. Cho-

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Cholelithiasis is more prevalent in European and American population as compared to the Asian and African population.<sup>5</sup> Gall stone formation is associated with other co-morbidities like metabolic syndrome, pregnancy, hemolytic anemia and Crohn's disease etc.<sup>6</sup>

There are different types of gall stones depending upon the contents and causes. The most common type of gall stone is the cholesterol gall stones making about 90% of the stone formation in the gall bladder.<sup>7,8</sup> Black pigment gall stones make 2% of the gall stones<sup>9</sup> and are related to the hemolytic anemias, Crohn's disease and cystic fibrosis. Brown pigment gall stones are associated with bile stasis and infections.<sup>10</sup>

The pathophysiology of the gall stone formation is a complex process which involves many factors. It is believed that biliary stasis and altered flow, hyperlipidemia and dysfunction of the sphincter of Oddi play role in the formation of gallstones.<sup>11,12</sup>

Hypothyroidism is one of the endocrine disorders affecting 3.7% of the people worldwide and is more common in females.<sup>13</sup> It is believed that hypothyroidism causes gall stone formation. There are several explanations for the cholelithiasis and hypothyroidism. The possible cause of stone formation in gall bladder in hypothyroid patients is the hyperlipidemia, motility disorders affecting the bile duct and sphincter of Oddi. Hypothyroidism in patients with cholelithiasis was explained in many studies having prevalence of 13 % to 24%.<sup>14,15</sup>

The aim of our study is to determine the prevalence of hypothyroidism in patients with cholelithiasis admitted in tertiary care hospital. This study will help us to know the prevalence of hypothyroidism in association with gender, age and BMI.

#### **Material and Methods:**

This was a descriptive cross sectional study conducted at Department of Surgery, PGMI Mardan Medical Complex/ MTI Mardan, Pakistan

from May 2018 to April 2019 for duration of one year. The sample size was 174, keeping 13%<sup>14</sup> proportion of hypothyroidism among patients with cholelithiasis, 95% confidence interval and 5% margin error using WHO sample size calculator. Consecutive non probability sampling technique was used for the sampling.

All the patients presenting with cholelithiasis diagnosed on the basis of ultrasonography with age 20 to 70 years, included in the study. Patients having history of thyroid surgery, pregnancy, hematological disorders especially hemolytic anemias and using drugs causing hypothyroidism like Amiodarone, Lithium, anti-depressants, Phenytoin or drugs causing gall stone formation like Estrogen, Fenofibrate, Gemfibrozil were excluded. Exclusion criteria were strictly followed to control the confounders and to exclude bias in the study results.

After obtaining permission from hospital ethical committee and taking consent from patients included in the study, 5 ml of blood was taken from all the patients admitted in the surgical ward for cholecystectomy and was sent to hospital laboratory for the detection of hypothyroidism. A patient was labeled as hypothyroid if the thyroid stimulating hormone was  $5.5\mu\text{IU/mL}$  or more with normal/low T3 and T4. All the investigations were done in same laboratory by a technician having experience of more than five years. All the data like age, gender, height weight, BMI, hypothyroidism were recorded in a pre-designed proforma.

All the data was analyzed in SPSS version 20. Mean and standard deviation was calculated for numerical variables and frequencies and percentages were calculated for qualitative variables. Chi square test for categorical variables was applied with p value of  $< 0.05$  as significant.

#### **Results:**

The mean and standard deviation of age, height, weight and BMI were  $41.66 \pm 13$ ,  $165.15 \pm 11.35$ ,  $68.17 \pm 11.95$  and  $25.69 \pm 7.19$  respectively. (table 1)

Table 1: Mean and standard deviation of quantitative variables of patients with cholelithiasis

Variables	Mean and Std. Deviation
Age (years)	41.66±13.81
Height (cm)	165.15±11.35
Weight (kg)	68.17±11.95
BMI (kg/cm2)	25.69±7.19

Table 2: Age group Distribution

Age Groups	Frequency	Percent
Age < 20 years	13	7.5
Age 21-30 years	20	11.5
Age 31-40 years	27	15.5
Age 41-50 years	82	47.1
Age > 50 years	32	18.4

Table 3: Frequency and percentage of hypothyroid patients

	Frequency (n=174)	Percent
Euthyroid	149	85.6%
Hypothyroid	25	14.4%

Table 4: Prevalence of Hypothyroidism in different age groups

Age groups	Euthyroid	Hypothyroid	Sig
Age < 20 years	12(92.3%)	1(7.7%)	0.28
Age 20-30 years	19(95.0%)	1(5.0%)	
Age 31-40 years	24(88.9%)	3(11.1%)	
Age 41-50 years	70(85.4%)	12(14.6%)	
Age > 50 years	24(75.0%)	8(25.0%)	

Table 5: Gender distribution of patients with Cholelithiasis

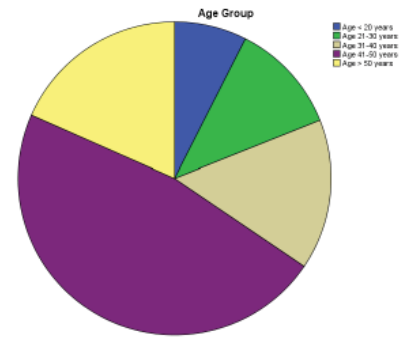
	Frequency	Percent
Female	97	55.7%
Male	77	44.3%

Table 6: Prevalence of Hypothyroidism in different age groups

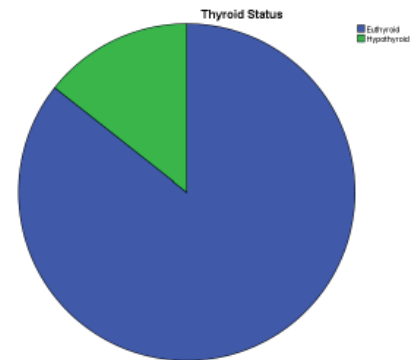
	Euthyroid	Hypothyroid	sig
Female	77 (79.4%)	20 (20.6%)	.008
Male	72 (93.5%)	5 (6.5%)	

Table 7: Prevalence of Hypothyroidism among different BMI groups

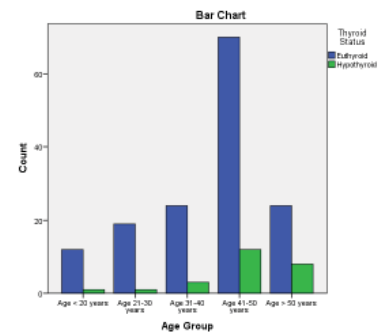
	Euthyroid	Hypothyroid	sig
BMI < 18kg/m2	26(89.7%)	3(10.3%)	0.674
BMI 18-24kg/m2	66(85.7%)	11(14.3%)	
BMI 25-30kg/m2	18(85.7%)	3(14.3%)	
BMI > 30kg/m2	35(79.5%)	9(20.5%)	



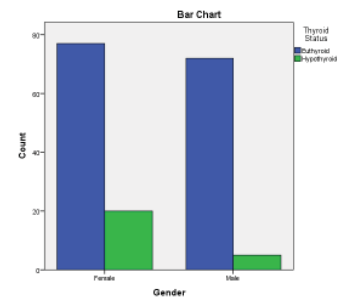
Graph1: Age relationship with cholelithiasis in the present study



Graph 2: Showing the relationship of thyroid status with cholelithiasis



Graph 3: Showing the relationship of hypothyroidism with cholelithiasis



Graph 4: Showing the gender relationship of hypothyroidism with cholelithiasis

Age group distribution: Out of 174 patients with cholelithiasis, 47.1% patients were from the age group 41-50 years, 18.4% were from the age group > 50 years, 15.5% were from the age group 31-40 years, 11.5% were from the age group 21-30 years and 7.5% were from the age group < 20 years.(table 2) (graph 1)

Frequency and percentage of hypothyroid patients: Out of 174-patients having cholelithiasis, 25-patients were hypothyroid making 14.4% while 85.6% patients were Euthyroid as shown in table-3 and graph 2

Prevalence of hypothyroidism in different age groups: The prevalence of hypothyroidism in age group above 50 years old patients with cholelithiasis was 25% while the age group 41-50 years was 14.6% hypothyroid. 11.1% patients were hypothyroid among the age group 31-40 years and 5% patients were hypothyroid in the age group 21-30 years and 7.7% patients with cholelithiasis were hypothyroid in the age group less than 20 years as shown in table-4 and graph-3.

Gender distribution of patients with Cholelithiasis: Out of 174 patients with cholelithiasis, 97(55.7%) were female patients while 77(44.3%) were male patients. (table 5)

Gender wise hypothyroidism distribution: Among 97-female patients 20(20.6%) were hypothyroid and among 77-male patients 5(6.5%) were hypothyroid. Hypothyroidism in male and female was statistically significant using Chi Square test with p value  $\leq 0.05$  s. (table 6) (graph 4)

Prevalence of Hypothyroidism among BMI groups: Hypothyroidism was more common in the patients having BMI more than 30kg/m<sup>2</sup>. Out of 35 (79.5%) patients with BMI > 30kg/m<sup>2</sup>, 9(20.5%) patients were hypothyroid. Prevalence of other BMIs i.e. BMI < 18kg/m<sup>2</sup>, BMI 18-24kg/m<sup>2</sup> and BMI 25-30kg/m<sup>2</sup> were (10.3%), (14.3%) and (14.3%) respectively. Statistically the results were insignificant but

the prevalence of hypothyroidism was more in obese patients. (table 7).

#### Discussion:

The risk factors for the formation of gall stones are the gender, age, obesity and co-morbidities.<sup>16</sup> Hypothyroidism is considered as one of the risk factors for the formation of the gall stones. According to a study by Watali YZ et al,<sup>17</sup> the prevalence of hypothyroidism was more in patients with cholelithiasis than the patients without cholelithiasis. Although it was not statistically significant but yet the prevalence of hypothyroidism was more in patients with gall stones. According to our study the prevalence of hypothyroidism in patients with cholelithiasis was 14.4%. The prevalence of hypothyroidism in our study showed resemblance with a study by Kotwani et al which also showed the prevalence of hypothyroidism in patients with cholelithiasis was 14.4%.<sup>18</sup> Other studies have shown different prevalence ranging from 8% to 24%.<sup>19,15</sup> According to our study 97(55.7%) patients were females and 77(44.3%) patients were males. Out of 97-female patients, 20-patients were hypothyroid making 20.6% of the female patients. Out of 77-male patients 5-patients had hypothyroidism making 6.5% of the male patients. According to a study by Bensal et al<sup>20</sup> there were 65% females and 35% males. The prevalence of hypothyroidism was more in female patients with cholelithiasis as compared to the male patients.

The prevalence of hypothyroidism in patients with cholelithiasis is greatly affected by the age of the patients. It is believed that the prevalence of hypothyroidism with cholelithiasis is more in old age. According to our study the prevalence of hypothyroidism was seen more in patients greater than 50 years. Honore LH et al<sup>21</sup> explained that the prevalence of hypothyroidism in patients with cholelithiasis was more prevalent in female patients having age more than 65-years.

Hyperlipidemia and obesity are considered as risk factors for the formation of cholesterol gall stones.<sup>22-24</sup> Patients with high BMI are more

prone to develop gall stones shown in different studies. As the hypothyroidism causes hyperlipidemia, thus risk of cholesterol type gall stones formation increases. In our study hypothyroidism was seen more in patients having BMI more than 30kg/m<sup>2</sup>.

### Conclusion:

This study was conducted to determine the relationship between hypothyroidism and cholelithiasis. It was concluded that hypothyroidism was more common in female, obese and elder patients. The gender distribution of the hypothyroidism in patients with cholelithiasis was statistically significant while all other variables were statistically not significant.

**Recommendation:** It is recommend that female, obese and elder patients having cholelithiasis should be screened for the thyroid dysfunction.

**Limitations:** This study has few limitations like gall stones types assessment was not done and relationship of hyperthyroidism with cholelithiasis was not studied.

**Conflict of interest:** None

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### Role and contribution of authors:

Dr. Mukhtiar Ali, discussion writing and proof reading

Dr. Bayazeed, introduction writing and data collection

Dr. Waseeq Ullah, data collection and interpretation

Dr. Abbas Ali Raza, data collection

Dr. Nazia Shahana, data analysis and reference writing

Dr. Jalil Khan, data analysis

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