

## Original research article

## A Prospective comparative study assess the Serum Iron Levels in Patients of Gall Bladder Stone Disease

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### Abstract

**Aim:** To determine the serum Iron Levels in Patients of Gall Bladder Stone Disease.

**Methods:** This Prospective study which was carried in the Department of General surgery, Government medical College, and Hospital, Bettiah, Bihar, India for 14 months, Patients diagnosed with gallstone disease admitted in various surgical wards and confirmed by ultrasonography, both male and female patients. Serum ferritins, serum cholesterol, serum iron along with other routine investigations were estimated in all 50 patients. Patients with gallstones were diagnosed with iron deficiency anemia based on hemoglobin levels, serum iron, and serum ferritin levels. Adult male with hemoglobin level <13 and adult female with <12 are diagnosed as anaemic. Gallstone patients were divided into anaemic and non-anaemic groups and compared with each other.

**Results:** Mean age of subjects was  $41.27 \pm 13.9$  years, range was 20–72 years and median age was 42 years. Majority of subjects were in the age group 20–30 years. In this study majority, i.e. 80% were females and 20% were males. Among females mean serum iron in subjects with iron deficiency was  $20.7 \pm 6.8$  and among males was  $43.2 \pm 5.2$ . Among females mean serum iron in subjects without iron deficiency was  $85.6 \pm 21.5$  and among males was  $102.7 \pm 23.2$ . Most of the patients with gallstone have serum iron level less than normal, and are anaemic. This association between low serum iron with anemia and gallstone disease was statistically significant in our study, P value of 0.002.

**Conclusion:** The low body store of serum iron is a risk factor for cholelithiasis in females and serum iron, serum ferritin may be used as marker of iron store so that low serum iron status could be diagnosed at early stage.

**Keywords:** Anemia, Cholelithiasis, Risk factor for gall stone, Serum iron, Serum ferritin

### Introduction

Cholelithiasis is a common abdominal disorder resulting in increasing hospital admissions. About 10-12% of adults develop gallstones.<sup>1</sup> The prevalence of common bile duct stones in patients with gallstones varies from 8 to 16%.<sup>2</sup> Pure cholesterol stones are uncommon and account for less than 10% of all stones. Whether pure or of mix nature, the common primary event in the formation of cholesterol stone is super saturation of bile with cholesterol. Super saturation almost always is caused by cholesterol hyper secretion rather than reduced secretion of phospholipids or bile salts.<sup>3</sup> Pigment stones contain less than 20% cholesterol and are dark because of presence of calcium bilirubinate. Black pigment stones are usually small, brittle, black and sometimes speckled. They are formed by super saturation of

calcium bilirubinate, carbonate and phosphate and occur most often secondary to hemolytic disorder such as hereditary spherocytosis and sickle cell anemia. Like cholesterol stones they are almost always found in gall bladder. Brown pigment stones are usually less than 1 cm in diameter, brownish-yellow and soft, often mushy. They may form either in gallbladder or in bile ducts, usually secondary to bacterial infection caused by bile stasis. Precipitated calcium bilirubinate and bacterial cell bodies compose the major part of the stone.<sup>3</sup> The role of iron in the pathogenesis of gallstone disease has not been well established so far. Iron deficiency has been shown to alter the activity of several hepatic enzymes, leading to increased cholesterol saturation of bile in gall bladder and hence promoting cholesterol crystallization.<sup>4</sup> Serum iron, total iron binding capacity and transferrin saturation are not good indicators of iron status in individuals. In infection free situation, serum ferritin is an ideal indicator for diagnosis of iron deficiency and response to iron therapy in a community.<sup>5</sup> If the prevalence of iron deficiency in a population must be described with a single number, serum ferritin should be used and complemented with haemoglobin in all programmed evaluations.<sup>6</sup> The serum iron concentration is found least in patients with pigment stones hence enforcing the role of iron in gall stone formation.<sup>7</sup> Nutritional anaemia is a major public health problem in India and is primarily due to iron deficiency. The old axiom that a typical gall stone sufferer is a fat, fertile, flatulent, female of fifty, is only partially true, as the disease is found in women soon after their first delivery and also in underweight and thin people.<sup>8</sup> While, searching for other established factors, recent studies have defined the role of trace elements such as iron in the formation of gallstones. Haemoglobin concentration alone cannot be used to diagnose iron deficiency. However, the concentration of haemoglobin should be measured, even though not all anaemia is caused by iron deficiency. The prevalence of anaemia is an important health indicator and when it is used with other measurements of iron status, the haemoglobin concentration can provide information about the severity of iron deficiency.<sup>9</sup> Serum ferritin will act as more specific indicator for iron deficiency anaemia.

### **Material and methods**

This Prospective study which was carried in the Department of General Surgery, Government Medical College, and Hospital Bettiah, Bihar, India for 14 months, after taking the approval of the protocol review committee and institutional ethics committee.

All patients with sonological evidence of gallbladder stones formed subjects for the study. A total of 50 patients fulfilling the criteria were included in the study.

### **Inclusion criteria**

Patients diagnosed with gallstone disease admitted in various surgical wards and confirmed by ultrasonography, both male and female patients: patients satisfying the above conditions and willing to give consent and participate in the study.

### **Exclusion criteria**

Patients who opt out of study and not giving consent for the study, patients diagnosed with cirrhosis of liver on ultrasound scan, patients with gallstone diseases due to hemolytic anemias, patients diagnosed clinically with Crohn's disease, and cystic fibrosis.

### **Methodology**

Serum ferritin, serum cholesterol, serum iron along with other routine investigations were estimated in all 50 patients. Patients with gallstones were diagnosed with iron deficiency anemia based on hemoglobin levels, serum iron, and serum ferritin levels. Adult male with hemoglobin level <13 and adult female with <12 are diagnosed as anaemic. Normal serum

ferritin levels in adult male average is 100  $\mu\text{g/L}$  (15–200  $\mu\text{g/L}$ ) and in female average is 30  $\mu\text{g/L}$  (12–150  $\mu\text{g/L}$ ). Normal serum iron levels in adult male is 60–160  $\mu\text{g/dL}$ , and in female 35–145  $\mu\text{g/dL}$ . Gallstone patients were divided into anaemic and non-anaemic groups and compared with each other. Data were analyzed with descriptive statistical principles.

### Results

Mean age of subjects was  $41.27 \pm 13.9$  years, range was 20–72 years and median age was 42 years. Majority of subjects were in the age group 20–30 years [Table 1].

In the study majority, i.e. 80% were females and 20% were males [Table 2].

Among females mean serum iron in subjects with iron deficiency was  $20.7 \pm 6.8$  and among males was  $43.2 \pm 5.2$ . Among females mean serum iron in subjects without iron deficiency was  $85.6 \pm 21.5$  and among males was  $102.7 \pm 23.2$  [Table 3].

Most of the patients with gallstone have serum iron level less than normal, and are anaemic. This association between low serum iron with anemia and gallstone disease was statistically significant in our study,  $P$  value of 0.002 [Table 4].

Mean serum cholesterol among those with iron deficiency was  $160 \pm 52.8$  mg/dL and among those without iron deficiency was  $168 \pm 43.0$  mg/dL. There was no significant difference in mean serum cholesterol between iron deficiency and no deficiency,  $P$  value of 0.507. There is no effect of anemia on serum cholesterol [Table 5]. Among females, 16% had raised serum cholesterol. Among males 8% had raised cholesterol.

Among females, 22.5% had decreased serum ferritin and among males 20% had decreased serum ferritin. There was no significant association between serum ferritin and gender,  $P$  value of 0.717 [Table 6].

There was significant association between low serum ferritin with anemia and gallstone disease in our study,  $P$  value of 0.003 [Table 7]

**Table 1: Age distribution of subjects with gallstone disease**

Age (years)	Number	%
20-30	13	26
30-40	12	24
40-50	12	24
50-60	8	16
60-70	3	6
Above 70	2	4
Total	50	100

**Table 2: Gender distribution of subjects with gallstone disease**

Gender	Number	%
Female	40	80
Male	10	20
Total	50	100

**Table 3: Mean serum iron levels with respect to gender and iron deficiency**

Serum iron	Female				Male			
	Mean	SD	min	max	Mean	SD	min	max
Iron deficiency	20.7	6.8	8	34	43.2	5.2	38	51
No iron deficiency	85.6	21.5	58	124	102.7	23.2	74	140

**Table 4: Association between anaemia and Serum iron levels in gallstone patients**

Serum iron	Hb			
	Anemia present		Anemia absent	
	Number	Percentage	Number	Percentage
Iron deficiency	41	82	20	40
No iron deficiency	9	18	30	60

**Table 5: Mean serum cholesterol levels with respect to iron deficiency anaemia**

Serum iron	S cholesterol				0.507
	Mean	SD	Min	Max	
Iron deficiency	160.5	52.8	85	300	
No iron deficiency	168.0	43.0	96	275	

**Table 6: Association between serum ferritin levels and gender in gallstone patients**

Serum ferritin	Gender			
	Female		Male	
	Count	%	Count	%
Decreased	9	22.5	2	20
Normal	31	77.5	8	80
$\chi^2=0.091$ , df=1, P=0.654	40		10	

**Table 7: Association between serum ferritin levels and anaemia in gallstone patients**

Serum ferritin	Hb			
	Anemia present		Anemia absent	
	Number	Percentage	Number	Percentage
Iron deficiency	41	82	20	40
No iron deficiency	9	18	30	60

## Discussion

Majority of the subjects were in the age group of 20–30 years. In the series of Ghosh et al. and Shenoy et al. the highest incidence was found in the age group of 41–50 years.<sup>10,11</sup> Tyagi et al. showed higher incidence in 30–40 years.<sup>12</sup> In Prasad et al. study majority of cases were in the age range of 20–40 years.<sup>13</sup> In the study, majority i.e. 80% were females and 20% were males. In Kumar et al. study 80% were females and 20% were males. Similar sex preponderance was noted by Tamhankar et al. and Ganey et al.<sup>14,15</sup> This study suggests that iron deficiency plays a significant role in super saturation of bile, leading to stone formation in the gall bladder. In study conducted by Prasad et al. 78% of the patients with gallstones had the value of serum iron less than normal. Most of the patients with gallstones have serum iron levels less than normal.<sup>13</sup> In a study by Kannan et al. showed that the gallbladder bile cholesterol level was significantly higher in anaemic patients due to low serum iron as compared to that of non-anaemic patients with normal serum iron levels leading to gallstone formation.<sup>16</sup> In a study by Kumar et al., found that low serum iron levels lead to bile super saturation with respect to cholesterol, which leads to gallstone formation.<sup>17</sup> There was no significant association between iron deficiency anemia and serum cholesterol in patients with gallstone disease. In study by Prasad et al. found that there is no effect of iron deficiency anemia on serum cholesterol which is similar to our study.<sup>13</sup> In a study by Kannan et al., no

statistically significant difference in serum cholesterol values of iron deficient and non-iron deficient groups, which is similar to our study.<sup>16</sup> In a study by Athar Parvez et al., there was no significant variation in the serum cholesterol of the two groups.<sup>18</sup> But in Halgaonkar et al. study, serum cholesterol levels were found to be raised in the majority of the patients.<sup>19</sup> There was significant association between serum ferritin and hemoglobin levels in patients with gallstone disease. In Prasad et al. study, 74% of patients with gallstones have normal value of serum ferritin; in this 48% are anaemic. Serum ferritin cannot be taken as a sole diagnostic tool in the diagnosis of iron deficiency anemia as its value can vary due to other causes such as iron therapy, hepatocellular disease, and inflammations (since cholecystitis is an inflammatory condition, this could be the reason for the high level of serum ferritin).<sup>13</sup> In the study by Athar Parvez et al. correlation between low serum ferritin and increase in cholesterol level in bile was established. This result gives impression that in reference to serum cholesterol, deficiency of serum ferritin will lead to increase in saturation of biliary cholesterol which may enhance gallstone formation.<sup>18</sup> There was no significant association between serum ferritin and gender. In Prasad et al. study, the number of females having normal serum ferritin levels (in both case and control groups) was more.<sup>13</sup>

### Conclusion

It was concluded that a low body store of serum iron is a risk factor for cholelithiasis in females and serum iron, serum ferritin may be used as marker of iron store so that low serum iron status could be diagnosed at early stage.

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