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To study serum iron levels in patients of gall bladder stone disease

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Abstract
Gallstone disease is a common gastrointestinal problem in day-to-day practice. The Old concept that a typical gallstone sufferer is fat, fertile, flatulent female of 50. This is partially true as the disease has been found in women soon after their first delivery who are thin and underweight and in males also. Conditions that favor the formation of cholesterol gallstones are super saturation of bile with cholesterol, kinetically favorable nucleation and presence of cholesterol crystals in the gall bladder long enough to agglomerate into a stone. Recent studies have defined the role of trace elements (Fe, Ca, Zn and Cu) and defective pH in the formation of gallstones.

The aim of the study was to correlate iron-deficiency anemia with gallstone disease. Serum cholesterol, iron and ferritin levels were compared in patients having gallstones and healthy individuals. A low serum iron level is a factor in bile super saturation with respect to cholesterol, leading to gallstone formation.

Keywords: gallstone, serum ferritin, bile cholesterol, anemia

Introduction
Gallstone disease is a common clinical entity affecting the adult population of both sexes. The earliest known gallstones date back to the 21st Egyptian dynasty discovered in the mummy of a priestess of Amenen (1085–945 BC). Gallstones are classified into either pure cholesterol stones, black or brown pigmented stones, or mixed stones. Conditions that favor the formation of cholesterol gallstones are super saturation of bile with cholesterol, kinetically favorable nucleation and presence of cholesterol crystals in the gall bladder long enough to agglomerate into stone. Recent studies have defined the role of trace elements (Fe, Ca, Zn and Cu) and defective pH in the formation of gallstones [1, 2].

Materials and Methods
One hundred cases: 50 patients suffering from Cholelithiasis confirmed by ultrasonography were included in this study. Fifty healthy volunteers were taken as the control group.

Inclusion criteria: All patients suffering from Cholelithiasis confirmed by ultrasonography were included in this study.

In the control group, the volunteers having the following disorders/disease were not considered: hematological disorders, cirrhosis of liver, cystic fibrosis, crohn's disease, familial hyperlipoprotenemia hyperlipoprotenimia type-3, pyruvate kinase deficiency,patients on long-term NSAIDS therapy, drugs causing gallstones(oestrone, clofibrate, cholesterol lowering agents) and pregnant females were also excluded. Serum iron was estimated by the Ferrozine kit method [3].

The normal reference values were supplied with the kit, for males (60–160 µg/dl) and for females (35–145 µg/dl). Serum cholesterol was estimated by the Enzopa kit based on the cholesterol oxidase/peroxidase method as devised by Allain *et al.* [4]. Based on the hemoglobin of the patients and control group, all cases were divided into two groups: Nonanemic: (i.e., hemoglobin>11 g%), and anemic (i.e., hemoglobin ≤11). Serum cholesterol, iron and ferritin contents of both groups were analyzed and compared with each other.

Table 1: Distribution of data according to age

S. no	Age group	Case anemic No. (%)	Case non-anemic No (%)	Control anemic No (%)	Control non-anemic No (%)
1	0–20	1 (2 %)	2 (4 %)	0 (0 %)	0 (0 %)
2	21–40	16 (32 %)	11 (22 %)	1 (2 %)	28(56 %)
3	41–60	11 (22 %)	10 (20 %)	2 (4 %)	19 (38 %)
4	> 61	1 (2 %)	0 (0 %)	0 (0 %)	0 (0 %)
5	Total no.	29	21	3	47
6	Mean	40.3		39.7	

Results
Table 1 shows the following:

1. The mean age in the case group (gallstones present) is 40.3 years (ranging from 0–60 years)
2. As compared to the control group (healthy volunteers) the mean age is 39.7 years (ranging from 20–60 years).
3. Both groups are comparable as far as age distribution is considered.
4. 54 % cases were in the age range 20–40 years and 42 % cases were in the age range 40–60 years.

Table 2 Distribution of serum iron according to anemia

S. no	Serum iron	Cases		Control	
		Anemic no. (%)	Non-anemic no. (%)	Anemic no. (%)	Non-anemic no. (%)
1	<Normal	26 (52 %)	13(26 %)	3 (6 %)	20 (40 %)
2	Normal	5 (10 %)	6 (12 %)	0 (0 %)	27 (54 %)
3	>Normal	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
4	Total	31	19	3 (0 %)	47

Table 2 shows the following:

1. 78 % of the patients with gallstones have the value of serum iron less than normal (normal value: 59—158 µg/dl).
2. 52 % of the patients in the case group whose value is less than normal are anemic.
3. 46 % of the healthy volunteers have value of serum iron less than normal (59–158 µg/dl).
4. 6 % of the healthy volunteers who have value of serum iron less than normal (59–158 µg/dl) are anemic.
5. Most of the patients with gallstones have serum iron levels less than normal, and they are anemic.

Table 3 Distribution of serum iron according to sex

S. no	Serum iron	Cases		Control	
		Male no. (%)	Female no. (%)	Male no. (%)	Female no. (%)
1	<Normal	8 (16 %)	31 (62 %)	4 (8 %)	19 (38 %)
2	Normal	5 (10 %)	6 (12 %)	8 (16 %)	19 (38 %)
3	>Normal	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
4	Total	13	37	12	38

Table 3 shows the following:

1. There are 62 % female patients with gallstone disease who have serum iron levels below the normal value (59–158 µg/dl).
2. There are 38 % females in the healthy volunteer group whose serum iron levels are below normal.
3. There are only 12 % female patients with gallstones whose serum iron levels are normal, which is 38 % females in the healthy control group.
4. Most of the patients with gallstone disease whose serum iron levels are subnormal are females.

Table 4 Distribution of serum cholesterol according to anemia

S. no	Serum cholesterol	Cases		Control	
		Anemic no. (%)	Non-anemic no. (%)	Anemic no. (%)	Non-anemic no. (%)
1	<Normal	13	5	1	18
2	Normal	15	15	2	38
3	>Normal	2	0	0	1

Table 4 shows the following:

1. 26 % of anemic and 10 % of non-anemic patients with gallstones have less than normal serum cholesterol levels, which is 2 % and 36 % in normal healthy individuals, respectively.
2. 30 % of anemic and 30 % of non-anemic patients with gallstones have one normal serum cholesterol level which is 4 % and 76 % in normal healthy individuals, respectively.
3. There is no effect of anemia on serum cholesterol.

Table 5 Distribution of serum cholesterol according to sex

S. no	Serum Cholesterol	Cases		Control	
		Male no. (%)	Female no. (%)	Male no. (%)	Female no. (%)
1	<Normal	4 (8 %)	13 (26 %)	1 (2 %)	8 (16 %)
2	Normal	8 (16 %)	23 (46 %)	11 (22 %)	29 (58 %)
3	>Normal	1 (2 %)	1 (2 %)	0 (0 %)	1 (2 %)

Table 5 shows the following:

1. 8 % of male and 26 % of female patients with gallstones have below normal serum cholesterol levels, which is 2 % and 16 % in normal healthy individuals, respectively.
2. 16 % of male and 46 % of female patients with gallstones have normal serum cholesterol levels, which is 22 % and 58 % in normal healthy individuals, respectively.
3. Serum cholesterol has no effect on sex in the formation of gallstones.

Table 6 Distribution of serum ferritin according to anemia

S. no	Serum ferritin	Cases		Control	
		Anemic no. (%)	Non-anemic no. (%)	Anemic no. (%)	Non-anemic no. (%)
1	<Normal	3 (6 %)	0 (0 %)	2 (4 %)	13(26 %)
2	Normal	24(48 %)	13 (26 %)	1 (2 %)	33 (66 %)
3	>Normal	5 (10 %)	5 (10 %)	0(0 %)	1(2 %)

Table 6 shows the following:

1. 74 % of patients with gallstones have normal value of serum ferritin; in this 48 % are anemic whereas 68 % in the control group have normal value and anemic are only 2 %.
2. In patients with gallstones most of them are anemic whereas in the control group most of them are non-anemic.

Table 7 Distribution of serum ferritin according to sex

S. no	Serum ferritin	Cases		Control	
		Male no. (%)	Female no. (%)	Male no. (%)	Female no. (%)
1	<Normal	3 (6 %)	2 (4 %)	5 (10 %)	10 (20 %)
2	Normal	10 (20 %)	32 (64 %)	7 (14 %)	27 (54 %)
3	>Normal	0 (0 %)	3 (6 %)	0 (0 %)	1 (2 %)

Table 7 shows the following:

1. In the case group, 6 % of male and 4 % of female patients have less than normal serum ferritin levels. This is 10 % and 20 % in the control group.
2. In the case group, 20 % of male and 64 % of female patients have normal serum ferritin levels. This is 14 % and 54 %, respectively, in the control group.
3. In the case group, 6 % of females have greater than normal serum ferritin levels. This is 2 % in the control group.
4. The number of females having normal serum ferritin levels (in both case and control groups) is more.

Discussion

Iron deficiency has been shown to alter the activity of several hepatic enzymes, leading to increased gall bladder cholesterol saturation and promotion of cholesterol crystal formation [5, 6]. Iron acts as a coenzyme for nitric oxide synthetase (NOS), which synthesizes nitric oxide (NO) important for the maintenance of gall bladder tone and normal relaxation [7, 8].

Alteration of motility of the gall bladder and sphincter of Oddi leading to biliary stasis results in cholesterol crystal formation, which has been reported with iron deficiency [9]. This study suggests that iron deficiency leading to anemia plays a significant role in super saturation of bile, leading to stone formation in the gall bladder.

The serum cholesterol of the anemic group was found to be similar to the non-anemic group. Iron deficiency probably alters the hepatic enzyme metabolism, leading to super saturation of gall bladder bile with respect to cholesterol irrespective of serum cholesterol levels, hence promoting the cholesterol crystal formation [10].

Conclusion

In the present prospective study of 100 cases, based on serum iron, serum cholesterol, serum ferritin and hemoglobin, the following conclusions were drawn.

1. Serum total cholesterol of the patients of cholelithiasis was not different from that of general population. There were no significant variations in the serum cholesterol contents of both the groups. Also, there was no significant variation of the above parameter in the male and female patients.
2. The low serum iron level in one or the other way was leading to bile super saturation with respect to cholesterol, which leads to gallstone formation.
3. 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 a inflammatory condition, this could be the reason for the high level of serum ferritin).

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