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Research Article

A PROSPECTIVE STUDY OF IRON DEFICIENCY IN GALL STONE DISEASE

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ABSTRACT

Background: A typical gall stone sufferer is a fatty, fertile, female of forty, is a primitive statement today, due its common occurrence in thin individual and also in post partum. So while searching for other parameters, iron deficiency was found to be a new parameter of interest in the etiology of gall stones.

Aims: The study was aimed at establishing the role of iron deficiency in the super saturation of bile with cholesterol and thus formation of gallstones.

Materials and Methods: 50 consecutive patients suffering from Cholelithiasis by Ultrasonography (USG) were divided into anemic and non-anemic groups, based on serum iron levels. Serum cholesterol and gall bladder bile cholesterol of both the groups were estimated. They were divided into two groups. Group A consisted of patients with normal serum iron levels (non-anemic) and group B, of patients with less than normal serum iron (anemic). Serum cholesterol and gall bladder bile cholesterol of both the groups were studied and compared.

Results: Out of the total 50 patients, 42 (84%) were females and 08 (16%) were males. The majority of patients 31 (62%) presented with all the three symptoms of cholelithiasis. 32 (76.1%) out of the total female patients were multipara. 42 (84%) patients had body mass index (BMI) more than normal and 10 (20%) had normal or decreased BMI. Serum total cholesterol of gall stone formers was not different from that of the general population. There were no significant variations in the serum cholesterol contents of both the groups ($P=0.367$, $t=0.91$). Also, there was no significant variation of the above parameter in the male and female patients ($P=0.082$, $t=1.77$).

Conclusion: The present study concludes that low serum iron levels lead to bile super saturation with respect to cholesterol, which leads to gallstone formation.

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INTRODUCTION

Gallstone disease has troubled human lives since time immemorial. Cholecystitis and cholelithiasis are the most common disorders affecting the biliary system. here are variations in incidence of gallstones according to geographical distribution. The incidence varies from country to country and even in different parts of the same country.¹

As the old axiom says that a typical gall stone sufferer is a fatty, fertile, female of forty, is only partially true with a female: male ratio of 3:1 up to age 50 years², as the disease has been found in women soon after their first delivery and also in underweight and thin people.³

Gallstone disease has also been reported in infants, thus no age is immune. Gallstones may produce symptoms or remain asymptomatic which are usually detected by abdominal ultrasound done for some other purpose. The presentation may range from flatulent dyspepsia and acute cholecystitis to its

complications like empyema, chronic cholecystitis, gangrene, fistula and gallbladder carcinoma.³

So while searching the literature for different factors, Iron deficiency was found to be new and interesting etiological factor in the formation of gall stones. Gallstones hence produced may be symptomatic or asymptomatic. Over half the cases are asymptomatic, usually detected by abdominal ultrasound. Today the incidence of gallstone disease has increased considerably with the invention of ultrasonography.⁴ Three conditions must be met to permit the formation of cholesterol gallstones. 1. Bile must be supersaturated with cholesterol.² Nucleation must be kinetically favorable.³ Cholesterol crystals must remain in the gall bladder long enough to agglomerate into stones.

Iron deficiency has been shown to alter the activity of several hepatic enzymes, leading to increased gall bladder bile cholesterol saturation and promotion of cholesterol crystal formation.⁴ Iron acts as a coenzyme for nitric oxide synthetase (NOS), and that is important for the maintenance of basal gall

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bladder tone and normal relaxation.⁵ It was found that iron deficiency resulted in altered motility of gall and sphincter of oddi (SO), leading to biliary stasis and thus increased cholesterol crystal formation in the gall bladder bile.⁶

The present study was conducted on the randomly selected individuals from 50 consecutive patients suffering from Cholelithiasis by Ultrasonography (USG) were divided into anemic and non-anemic groups, based on serum iron levels.

MATERIALS AND METHODS

The study was conducted over a period of three year, from February 2013- January 2016. The study protocol was approved by the review board of our institute for ethical research. It was a Prospective analysis. The patients were selected, based only on the USG confirmation of their gall stones, irrespective of their age, sex, physique, parity, etc. Only those patients were included, whose serum as well as bile could be procured for analysis.

Patients who underwent Cholecystectomy open or laparoscopic, but whose bile sample was not available for analysis and patients with empysematous gall bladder were also excluded. Thus their bile and serum samples were collected. All the numbered samples with less than normal serum iron (n=26) were put in the anemic group, B and all the samples with normal serum iron (n=24) were put in the non anemic group, Group A. Serum iron was (60-160 µg/dl) and for females (35-145 g/dl).

During the operation for cholecystectomy, bile was aspirated with an aspiration needle mounted on a sterilized syringe. The aspiration needle was passed obliquely into the fundus of gall bladder and as much of bile as possible, was withdrawn from the gall bladder. Bile was kept in a sterile labeled container and carried to the Biochemistry Department for analysis. Serum cholesterol and gall bladder bile cholesterol of all the patients were estimated. Bile was first subjected to the Folch method to extract lipids and then the cholesterol contents were estimated as for serum cholesterol.

Statistical analysis

Data amongst the two groups were subjected to statistical analysis using students' t-test. The P-value

RESULTS

Out of the total 50 patients, 42 (84%) were females and 08 (16%) were males. The majority of patients 31 (62%) presented with all the three symptoms of cholelithiasis i.e. pain in the right upper quadrant, nausea/vomiting and flatulent dyspepsia. Pain was the most consistent symptom present in 48 (96%) patients.

Table 1 Showing the basic characteristics for the study group

| Individuals | No (%) | Range (µg/dl) | Mean ± S.D |
|----------------|-----------|---------------|------------|
| Males (n=8) | 8 | 40-140 | 110 ± 30 |
| Non-anemic | 7(87.5%) | 90-140 | 118 ± 18 |
| Anemic | 1(12.5) | - | 30 |
| Females (n=42) | 42 | 5-150 | 50 ± 32 |
| Non-anemic | 20(47.61) | 40-150 | 78 ± 32 |
| Anemic | 22(52.38) | 5-35 | 24 ± 8 |

32 (76.1%) out of the total female patients were multipara. 42 (84%) patients had body mass index (BMI) more than normal and 10 (20%) had normal or decreased BMI. Normal BMI means values between 19.1-24.9.

Serum total cholesterol of gall stone formers was not different from that of the general population. There were no significant variations in the serum cholesterol contents of both the groups (P=0.367, t=0.91). Also, there was no significant variation of the above parameter in the male and female patients (P=0.082, t=1.77).

The gall bladder bile cholesterol was significantly higher in the anemic individuals, as compared to that of the non-anemic ones (P<0.0001, t=4.2).

DISCUSSION

The present study titled "A prospective study of iron deficiency in gall stone disease." conducted on the randomly selected individuals, suffering from gall stone disease, to decipher the facts regarding the etiology of gall stone formation and the role of iron deficiency anemia in gall stone formation.

Out of the 50 gall stone patients included in the present study, 42 (84%) were females and 08 (16%) were males. The majority of patients 31 (62%) presented with all the three symptoms of cholelithiasis i.e. pain in the right upper quadrant, nausea/vomiting and flatulent dyspepsia. Pain was the most consistent symptom present in 48 (96%) patients, supporting the age old axiom that gall stone formation is most common in the female population. The increased prevalence of gall stone formation in females could be attributed to the fact, that anemia is more common in females than males, as 22 (55%) females were observed to be anemic, as compared to 1 (10%) male

This male to female ratio of 1:5 observed in the present study was different from that of Pima Indians (1:17)⁷ and Pakistanis (1:3).⁸ This sex-related difference showing more prevalence of cholelithiasis in females could be linked to pregnancy and female sex hormones and also to iron deficiency anemia now.

All the females, both anemic (n=22) and non anemic (n=20) included in the present study, the number of multipara females (n=19 and n=12 respectively) suffering from gall stones was more than that of primipara (n=2 and n=8 respectively) and nullipara (n=1 and n=2), respectively, hence suggesting, that parity plays a significant role in gall stone formation.

The percentage of multipara female patients was more in the anemic 19 (86.3%) group than in the non anemic 12 (60%) group, again reinforcing the fact that anemia contributes to gall stone formation.

All non anemic gall stone sufferers (n=27) had a high average serum iron content of 98 ± 25 µg/dl, as compared to anemic ones (n=23), where average serum iron was 27 ± 4 µg/dl. The corresponding values for serum cholesterol were observed to be 180 ± 34 mg% and 170 ± 42 mg% and that for gall bladder bile cholesterol were 0.76 ± 0.3 g% and 1.4 ± 0.44 g%, respectively.

There was no significant variation (P=0.396) in the serum cholesterol of the two groups, whereas gall bladder bile cholesterol was significantly increased (P<0.0001) in the anemic, than in the non anemic group, thus suggesting that

anemia may be contributing to the super saturation of gall bladder bile with respect to cholesterol independent of serum cholesterol levels.

Probably anemia, obesity and sex hormones are independent risk factors operating for the causation of gallstones and if present together, they produce synergistic effects.

CONCLUSION

Low serum iron levels lead to bile super saturation with respect to cholesterol, which leads to gallstone formation.

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