Role of Serum Iron and Serum Calcium in Patients of Cholelithiasis.

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ABSTRACT

Background: Gangetic plains are known to have a very high incidence of cholelithiasis, the eiopathogenesis of which cannot be ascertained. **Aim:** to conduct a study to find a correlation, if any between the incidence of gallstone disease and the serum Iron and serum Calcium levels of patients and compare it with controls. **Methods:** 50 patients and 50 controls were taken and serum Iron and serum Calcium of both were evaluated. The distribution of age, sex and gender were taken as factors. **Results and conclusion:** The number of female patients was higher than the males but no strong association could be proven in the study. Among the symptoms dyspepsia had the highest incidence but could not be taken as a reliable marker for the diagnosis of cholelithiasis clinically. Hence, ultrasonography remains a very important tool for the diagnosis of the diasease .The role of serum Iron and serum Calcium in the etiopathogenesis could not be established. There was however a strong correlation of previous surgery in the formation of new gallstones .The family history was a strong factor for the formation of new gallstone disease however, the association was not established in this study. Gallstone disease had stronger association with anaemia than with serum Serum Iron. Calcium levels were comparable between the cases and the controls.

Keywords: Cholelithiasis, Serum Iron, Serum Calcium.

INTRODUCTION

Cholelithiasis is one of the most common human ailments which has been documented since ancients times .The result of epidemiological studies carried out in different countries show that prevalence rate of gallstone disease is between 10 - 25 % , which may rise by 1% every year and can become 60 % after 80 years.[1-3]

Inspite of its high prevelance in the western world and this part of the country (North India), the exact aetiopathogenesis of gallstone disease has not been established. Various factors like infection, metabolic changes and bile stasis in the gallbladder have been implicated. Three conditions must be met for the formation of gall bladder stones. These are - super saturation of bile with cholesterol, kinetically favourable nucleation and the persistence of cholesterol crystals in gall bladder long enough to agglomerate into stones.[4] There exists a possibility ,that alteration of serum Iron and serum Calcium may have a role in the formation of gallstones.

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Views, that increase and / or decrease of serum iron and serum calcium levels may play a role in formation of gallstones,[5] exists, and needs further investigations, hence the present study was planned . We evaluated 50 patients of cholelithiasis and 50 controls to find, correlation, if any, between the serums levels of Iron and Calcium and gallstone disease.

Aims and Objectives

1. To estimate serum iron levels in patients of cholelithiasis and controls.
2. To estimate serum calcium levels in patients of cholelithiasis and controls.
3. To undertake a comparative evaluation of serum iron and serum calcium levels in patients of cholelithiasis and controls.
4. To study the significance of serum iron and serum calcium levels in the occurence of cholelithiasis , and to find the role , if any, in aetiopathogenesis of cholelithiasis.

MATERIALS AND METHODS

The present prospective study was conducted in the Department of Surgery and Biochemistry of Sri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly, Uttar Pradesh, India.

50 consecutive patients of Ultrasonographically proven cholelithiasis, admitted in the surgical wards

with effect from December 2015, were included in this study. Patients of both laproscopic cholecystectomy (LC) and open cholecystectomy (OC) were included in the study group. Further 50 controls werelalso taken. The control group were taken from the patient attendants and paramedics and nursing staff and patients that underwent routine checkups, who had no history / family history of cholelithiasis. The control group had ultrasound abdomen with routine blood test done including serum Iron and serum Calcium levels. Due written informed consent was taken from both patients as well as controls. A similar prospective study has has not been conducted in the Rohailkhandregion. We therefore took a sample size 50 patients and 50 controls.

The patients and controls were matched for their age. Sera of all these 50 patients and 50 controls were examined for serum iron and serum calcium levels. Routine blood investigations including a complete blood count, renal function tests and liver function tests were done as a part of a package available at our hospital. A detailed personal and family history was taken from all patients and controls which included family history of cholelithiasis, previous surgery, any childhood illness and diseases that run in the family. General and local examination of each case and control was done and any lump, in right hypochondrium, was noted.

The number of patients and controls were matched to divide into male and female. The lower cutoff for heamoglobin level was 10 g/dl for females males and 11 g/dl for males.

The data was charted and analysed by standard statistical methods.

Exclusion Criteria
Patients having following disorders were excluded from the study by history / clinical examination and other relevant investigations.
1. Bone tumors
2. Hyperparathyroidism
3. Renal failure
4. Rickets
5. H/O Vitamin D deficiency or Iron Deficiency (taking supplementations)
6. Empyema gall bladder

The above entities / diseases were excluded by history / clinical examination.
Based on serum Iron levels, subjects will be divided in the following groups –

Patients
1 Patients having serum iron within normal limit (60 - 160 micg/dl for males 35-145 micg/dl for females)
2 Patients having serum iron less than 60 micgms/dl for males and 35 micgm/dl for females
Controls

3 Controls having serum iron within normal limit (60 - 160 micg/dl for males 35-145 micg/dl for females)
4 Controls having serum iron less than 60 micgms/dl for males and 35micgm/dl for females
Based on serum calcium levels, subjects were divided in the following groups –

Patients
5 Patients having serum calcium within normal limits (8.7 – 11 mg/dl)
6 Patients having serum calcium less than 8.7 mg/dl Controls
7 Controls having serum calcium within normal limits
8 Controls having serum calcium less than 8.7 mg/dl

Analysis
Statistical testing was conducted with statistical package for social science system version SPSS 17.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. The comparison of normally distributed continuous variables between the group were performed using the Student t test .Nominal categorical data between the groups were compared using Chi-squared test of Fischer's exact test as appropriate. $P < 0.05$ was considered statistically significant.

RESULTS & DISCUSSION

Gall stone disease is a common surgical problem in day to day practice. We conducted a prospective, pilot study to investigate the correlation of serum Iron and serum Calcium levels in patients of cholelithiasis.

There was definite clustering of cases around 4th and 5th decade as evident from data. The mean age of the cases was 40.04 ± 15.12 years (mean ± SD) and that of controls was 42.38 ± 12.05 years (mean ± SD) (p = 0.625). 62 % of the cases were between the ages of 31 and 60 years depicting peak in the middle age and elderly. 76 % of the control group was between this age group which was appropriate for matching the data for age. 10 % cases were between the ages of 11 and 20 years. 84% cases were between the ages of 21 to 60 years.

There were 12 (12%) patients who had age more than 60 years at the time of presentation with eldest being 83 years and only 1 (1%) patient falling into 2nd decade with age of 20 years. These findings were similar to those observed in epidemiological study of cholelithiasis (Jayanthi, 1996).[6]

The prevalence of gallstone disease was more in females as compared to males, with 28 (56 %) being females and the rest 22 (44 %) were male:

Female to male ratio was of 1.27 : 1 . This is not in accordance with the previous studies which stated a high prevalence of cholelithiasis in females which was associated to the effects of estrogen and progesterone on the biliary tract. Estrogenic

influences increase the effect of hepatic lipoprotein receptors and stimulate hepatic hydroxyl methyl glutaryl coenzyme A (HMG Co-A) reductase activity. Consequently, together cholesterol uptake and biosynthesis are increased leading to super-saturation of bile with cholesterol and helping in formation of gallstones. Progesterone alters the sphincter of Oddi and gallbladder function ultimately causing a derangement in bile flow dynamics. Even though, the effects of progesterone on the biliary tract have been implicated in the increased incidence of gallstones among the women, the specific effects of prolonged elevated levels of progesterone on the sphincter of Oddi and bile flow dynamics are still incompletely understood. There was a great predilection for stone formation in multiparous females (90.3%) as compared to that of primipara (8.5%) and nullipara (1.2%). Pregnancy favours the formation of gallstones through the hormonal influence on bile composition (increased biliary cholesterol secretion, diminished and disturbed bile acid pool).

Estrogen induces an increased input to the hepatic free cholesterol pool by up-regulating the low density lipoprotein. Decreased gallbladder motility during third trimester of pregnancy and an altered function of gallbladder mucosa that may favour nucleation and growth of stones.

Pain which was colicky in nature, intermittent and felt in the right hypochondrium was the most consistent symptom. This pain increased on taking fatty food and relieved on taking antispasmodic medications. Sometimes, a constant dull ache was felt in epigastric region which decreased on taking analgesics. However, such association was not investigated in this study.

In the 'others 'category, 64% of cases and 72 % of controls showed no symptoms. The number of smokers in the case and control group were comparable, 12 and 10 % respectively. However, 16 % of diabetic cases and only 8 % of diabetic controls with no cholelithiasis were found. The number of hypertensive cases were 8 % and the number of hypertensive controls were 10 % respectively. There was one patient with Chronic kidney disease and one patient of Chronic obstructive pulmonary disease in the case group. There were no patient with these diseases in the control group.

Flatulent dyspepsia was the most common presenting symptom, followed by vomiting. Half the patients in the case group gave a positive history of dyspepsia. In the control group only 32 % complained of dyspepsia not associated with other symptoms of cholelithiasis. Since the control group were also ultrasonologically proven not to be cases of cholelithiasis, the importance of taking dyspepsia alone as a strong indicator for cholelithiasis is not recommended (p = 0.067).

Various other authors have described similar symptomatology in their studies, with pain being the most common presentation in gallstone disease.

94 % of cases and 96 % of the controls had a normal liver on ultrasonology. The liver was scanned for liver echotexture and dilated intrahepatic bile radicals. 6 %of cases and 4 % of controls had fatty liver.

While studying the pathogenesis of gallstone formation, certain known risk factors can be listed like elderly age, female sex, obesity and rapid weight loss, cirrhosis and different diet linked issues. On seeking for other risk factors, latest studies have defined the role of trace elements like Iron and Calcium which might play a definitive role in the formation of gallstones. In our study, the details of risk factors and drugs taken were cautiously taken. The history of eostrogen and progesterone intake was affirmed. None of the females were using any of the two.

Many investigators have consistently reported that super saturation of bile with cholesterol occurs in most patients with gallstones however, the mechanism of initiation of gallstone formation was not clear in these patients. Normally gall bladder mucosa absorb a part of the calcium in bile, resulting in its low concentration level in bile compared to that in serum. In present study the mean calcium levels for cases were 9.00 ± 0.92 mg / dl and the mean for controls was 9.15 ± 0.77 mg / dl. 2 % of cases had a higher than normal calcium level and 44% had less than the lower set point. In the control group, 2 % has more than normal calcium level and 40% had less than the lower set point for calcium (p = 0.920).

Serum Iron was calculated in all cases and controls. The mean Iron in cases was 71.18 ± 26.44 (mean ± SD) micg/dl. The mean Iron in the control group was 75.08 ± 18.57 (mean ± SD) micg/dl (P value = 0.433). For the females the mean serum Iron value in the case group was 71.18 ± 26.44 (mean ± SD) micg/dl. The mean serum Iron value in the females of control group was 75.08 ± 18.57 (mean ± SD) (p = 0.433) micg/dl. The mean Iron level for males in the case group was 76.00 ± 22.88 micg/dl and the mean Iron level for controls was 75.80 ± 18.68 micg/dl (p = 0.806) . For the males, 22.7 % cases had serum Iron less than lower set point while in the control 16 % males had Iron less than lower set point (p = 0.715). This observation was not found in agreement with the findings of Verma et al.[7]

Iron deficiency alters the activity of several hepatic enzymes, leading to increased gallbladder bile cholesterol saturation and promotion of cholesterol crystal formation.[8] It is also suggested that iron deficiency alters the activity of several hepatic enzymes. They concluded that consumption of diet rich in carbohydrates but deficient in iron resulted in altering of hepatic metabolism of cholesterol that might be important in gallstone formation.

Previously researchers had concluded that iron deficient diet altered hepatic enzyme metabolism which in turn increased gallbladder bile cholesterol and promoted cholesterol crystal formation.[9]

Thus, iron deficiency was not found to have a major role in gallstone formation. The difference in serum iron contents of male and female gall stones patients was not found to be statistically significant with male patients having more serum iron levels (p<0.005). Thus, subclinical anaemia although being more prevalent in females, was not statistically significant in this study. It was probably related to better nutritional status in our female patients.

On a close examination, it can be concluded that the occurrence of gall stones was more common in females 56 % versus 44 % in males. In females, cholelithiasis did not have a predilection for iron deficient patients as compared to patients with normal serum iron. These findings were not in accordance to literature. We therefore conclude, that iron deficiency although had been proven by other studies to lead to gall bladder stasis, causing increased cholesterol crystal formation in bile within the gall bladder,[10,7] was not a statistically significant factor in our study. This however may be due to the small sample size.

These findings were also not in accordance with those of Kumar et al. (2006) who also observed in their study that iron deficiency altered the activity of several hepatic enzymes leading to increased gallbladder bile supersaturation and promotion of cholesterol crystals.

A deficiency in serum calcium causes deranged function of Nitric Oxide Synthase (NOS) resulting in altered gallbladder motility, leading to biliary stasis and subsequently increased crystal formation in bile.[7] Nitric Oxide (NO) is important in maintenance of basal gallbladder tone and normal relaxation.

The serum calcium levels in patients and controls showed no statistically significant difference. The values in both groups were comparable.

The history of past surgery was also noted. A strong positive correlation was found in cases having past history of surgery (p = 0.006). This history was noted for any previous abdominal surgery, gynaecological or obstretic surgery, appendectomy, otherwise. 16 % of the cases of cholelithiasis had a positive past history of surgery. In the control group the frequency was 0 %.

Association to a particular blood group was not found.

CONCLUSION

After statistical analysis of the data collected from 50 patients and 50 controls we conclude the following:

1. The number of female patients was higher than the males but no strong association could be proven in the study.

2. Among the symptoms dyspepsia had the highest incidence but could not be taken as a reliable marker for the diagnosis of cholelithiasis clinically hence, ultrasonography remains a very important tool for the diagnosis of the diasease.

3. The role of serum Iron and serum Calcium in the etiopathogenesis could not be established.

4. There was however a strong correlation of previous surgery in the formation of new gallstones.

5. The family history was a strong factor for the formation of new gallstone disease however, the association was not established in this study.

6. Gallstone disease had stronger association with anaemia than with serum Iron.

Serum Calcium levels were comparable between the cases and the controls.

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