CROSS SECTIONAL OBSERVATION STUDY ON INVESTIGATING THE LIFESTYLE CHANGES AND RISK FACTORS INFLUENCING GALLSTONE DISEASES

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ABSTRACT

Gallstone Disease (GSD) is often thought to be a major affliction in modern society. However, gallstones must have been known to humans for many years, research evident that gallbladder stone reports in the back of 1000 BC. This disease is however, a worldwide medical problem, even though there are geographical variations in gallstone prevalence. Gallstones are becoming increasingly common; they are seen in all age groups, but the incidence increases with age. Gallstones are composed mainly of cholesterol, bilirubin, and calcium salts, with smaller amounts of protein and other materials. Cholesterol super saturation, the essential requirement for cholesterol gallstone formation, might occur via excessive cholesterol biosynthesis, which is the main lithogenic mechanism in obese persons. High biliary protein and lipid concentrations are risk factors for the formation of gallstones. The prevalence of cholelithiasis may vary and it has been reported up to 2 to 29% in India and it because of difference with interstate and interregional. Hence the main aim of the present investigation is to find out the recent risk factor that contributes to the emergence of the gallstone and its biological significance. Cross sectional observational study involving 50 Patients with the diagnosis of GSD visiting in OPD of the Government Peripheral Hospital, Chennai by using questionnaire to collect required data. Results of the study clearly depicts that the females are more prone to the GSD with increases occurrence on age between 51 to 60 years. Influence of mixed diet has shown higher prevalence and along with higher occurrence on the chicken protein diet consumption. It was also observed that higher risk associated with overweight and sedentary life style individuals. It was concluded that alcohol consumption, smoking habits and history of diabetes are linear relationship in gallstone formation. Further this study provided valuable information on current life style risk factors associated with the morbidity of the GSD and also enriches the knowledge on prevention of the same in near future.

KEY WORDS: *Gallstone disease, Cholelithiasis, Observational study, Life style risk factors, Cholesterol, Diet consumption*

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1. Introduction

Gallstones constitute a significant health problem in developed societies, affecting 10% to 15% of the adult population, meaning 20 to 25 million Americans have (or will have) gallstones [1-3]. The resultant direct and indirect cost of gallbladder disease represents a consumption of ~$6.2 billion annually in the U.S., constituting a major health burden that has increased more than 20% over the last 3 decades [4-5]. With an estimated 1.8 million ambulatory care visits each year, gallstone disease is a leading cause for hospital admissions related to gastrointestinal problems [7].

Diseases of the gallbladder commonly manifest as gallstones and gallbladder cancer. To identify risk factors in a given population, epidemiological studies must first define the frequency of disease. Studies employing necropsy surveys or healthcare databases carry biases by their implicit nature: being postmortem or requiring biliary symptoms/complications, respectively [8]. Another potential measure of disease burden, the frequency of cholecystectomy, is a limited marker for the prevalence of gallstones, as the perceived threshold for surgery and patient access to care differ greatly [9].

Gallstones are hardened deposits of the digestive fluid bile, that can form within the gallbladder. They vary in size and shape from as small as a grain of sand to as large as a golf ball [10]. Gallstones occur when there is an imbalance in the chemical constituents of bile that result in precipitation of one or more of the components. Gallstones are composed mainly of cholesterol, bilirubin, and calcium salts, with smaller amounts of protein and other materials [11].There are three types of gallstones [12] (i) Pure cholesterol stones, which contain at least 90% cholesterol, (ii) pigment stones either brown or black, which contain at least 90% bilirubin and (iii) mixed composition stones, which contain varying proportions of cholesterol, bilirubin and other substances such as calcium carbonate, calcium phosphate and calcium palmitate [13]. Brown pigment stones are mainly composed of calcium bilirubinate whereas black pigment stones contain bilirubin, calcium and/or tribasic phosphate [14]. In Western societies [15] more than 70% of gallstones are composed primarily of cholesterol, either pure or mixed with pigment, mucoglycoprotein, and calcium carbonate [16]. Pure cholesterol crystals are quite soft, and protein contributes importantly to the strength of cholesterol stones [17].

Gallstones occur in about one third of the patients having liver cirrhosis. Pigment gallstones are the most frequent type, while cholesterol stones represent about 15% of all stones in cirrhotics. Increased secretion of unconjugated bilirubin, increased hydrolysis of conjugated bilirubin in the bile, reduced secretion of bile acids and phospholipids in bile favor pigment lithogenesis in cirrhotics. Gallbladder hypomotility also contributes to lithogenesis. Gallstone prevalence increases with age, with a ratio male/female higher than in the general population. Chronic alcoholism, viral C cirrhosis, and non-alcoholic fatty liver disease are the underlying liver diseases most often associated with gallstones. Gallstones are often asymptomatic, and discovered incidentally. If asymptomatic, expectant management is recommended, as for asymptomatic gallstones in the general population [18].

Treatment includes bile salt therapy i.e. Ursodeoxycholic acid (UDCA) and chenodeoxycholic acid (CDCA) decrease HMG-CoA reductase activity which in turn decreases hepatic cholesterol synthesis. It also causes dispersion of cholesterol and retards cholesterol crystal nucleation. Simvastatin, an HMG-CoA reductase inhibitor has also been tried in oral dissolution of gallstones by virtue of inhibiting cholesterol synthesis. The disadvantages of bile salt therapy or using Simvastatin is that there is recurrence after 5 years in about 50% of cases. This type of therapy is suitable only for small, cholesterol, non-calcified stones in a functioning gall bladder. Recurrence rate is high thus requiring prolonged costly therapy. Only 10% of all patients with gallstones are suitable for this type of therapy [19].

2.Materials and Methods

2.1. Study design

Cross- Sectional study conducted in Government Peripheral Hospital, Anna Nagar, Chennai,Tamil Nadu, India

2.2. Study Approval

This study was approved by Institutional Ethics Committee (IEC No: GSMCCH-ME-2/028/2019) and registered in Clinical Trial Registry India (CTRI/2019/07/020146).

2.3.Sampling procedure

Sample size for this study was 50 patients with the diagnosis of GSD in Department of Medical Gastroenterology OPD at Government Peripheral Hospital, Anna Nagar, Chennai during the period of July 2019 to October 2019. Simple randomized sampling method are followed. Inclusion criteria consisted of all stable patients with the diagnosis of GSD ascertained ultrasonography or having a medical history of cholecystectomy for GSD between the age group of 18-60 years. Exclusion criteria was patient who were not willing for study and seriously ill patients. Informed consent form was attached in the questionnaire. The purpose of this study was fully explained to the patients and data were collected by interviewing questionnaire.

2.4. Data Collection

Data collected from all the participants including demographic characteristics like age, gender, literacy, occupation, marital status. Lifestyle variables (alcohol consumption, smoking habit, physical exercise) and dietary pattern (vegetarian/non-vegetarian, which type of meat more taken, fasting history) also recorded. Height and body weight were measured and body mass index (BMI) was calculated. BMI was calculated According to Indian guidelines (normal 19-24, overweight 25-29, obese above 30). History of diabetes, Coronary Artery Disease (CAD), Dyslipidemia, Cholecystitis (inflammation of gall bladder), Cholecystectomy, laboratory values (lipid profile), In case of female's parity (nulliparous/ primiparous/multiparous), history of estrogen therapy and birth control pills retrieved were recorded from case sheets.

2.5. Statistical Analysis

All these data entered in Microsoft excel and analysis was done by SPSS statistics version 26. Percentage, Chi-square test and logistic regression were used in final analysis.

3.Results

3.1. Result analysis on the impact of primary factors that influence the GSD

The current study shows that among 50 cases 30 cases (60%) were females and 20 cases (40%) were males and patients under the age group 51-60 years (40%) are mostly affected in gallstone diseases. According to this study 14 cases (28%) belongs to House wife and 45 cases (90%) were married and 5 cases (10%) were unmarried. 35 cases (70%) were noted in mixed diet and 15 cases were noted in vegetarian diet. High incidence of cases 68% was noted in irregular diet timing and the disease occurred to the people who consumed non-veg weekly once 71% were noted. The patients who consumed chicken meat had high incidence 60 % were noted. 20 cases (40%) were noted in no fasting category and,14 cases (70%) were noted under weekly once fasting category. 37 cases (74%) were noted in Non-alcohol consumption and 13 cases (26%) were noted with alcohol consumption.

3.2. Significance of Sedentary habituation and Co-morbidity in GSD

The incidence of daily alcohol consumption was noted about 54%. In smoking category 10 cases (20%) were noted in smoking habit and current smokers affected in 4 cases (40%), chain smokers were noted in 1 case (10%), previous smoker affected in 3 cases (30%) and occasional smoker affected in 2 cases (20%). In physical exercise category, patients were affected with physical exercise was about 32 % in 16 cases. The incidence of patients with daily physical exercise were noted in 15 cases (94%).18 cases (36%) were comes under no morbidities. 10 cases (20%) were noted in diabetes mellitus. 6 cases (12%) came under both diabetes mellitus and hypertension. 3 cases (6%) were noted in both obesity and dyslipidaemia. 9 cases (18%) were noted as hypertension and 1 case (2%) was noted in typhoid fever.

3.3. Influence of Hormones and Limits of serological index in patients with GSD

Out of 30 cases of females, 19 cases (63%) were multiparous and 2 cases (7%) came under estrogen therapy. 34% cases history of usage of birth control pills were noted. Among 50 cases, 33 cases (66%) were noted with normal bilirubin level and 17 cases (34%) were noted with abnormal bilirubin level. 37 cases (74%) were noted with abnormal SGOT and 13 cases (26%) were noted with normal SGOT level. And the level of SGPT was abnormal in 26 cases (52%) and normal level was noted in 24 cases (48%). Normal ALP level was noted in 32 cases (64%) and abnormal ALP was noted in 18 cases (36%). According to this study, 47 cases (94%) were noted with normal total protein level and 3 cases (6%) were noted with abnormal total protein. All the cases (100%) were noted with normal albumin and 27 cases (54%) were

noted with normal globulin level and 23 cases (46%) were noted with abnormal globulin level. The above table showed the most prevalence of the disease with over weight (80%), 12 % with normal BMI and 8% with obese. Table showed that relationship between gallstone diseases and risk factors. Occupation, type of meat, parity, birth control pills were all significantly (p-value < 0.05) associated with GSD.

4.Discussion

Since most gallstones are asymptomatic, it is essential to define exactly which symptoms are caused by gallstones: true biliary pain and/or complications, versus nonspecific abdominal complaints including dyspepsia [20]. Gallstone-associated pain seems to follow a certain pattern in most patients [21]. The frequency of gallstones increases with age, escalating markedly after age 40 to become 4 to 10 times more likely in older individuals [22]. The stone type also changes with age: initially being composed predominantly of cholesterol (corresponding to an increased cholesterol secretion into and saturation of bile) but in late life tending to be black pigment stones. Further, symptoms and complications increase with age, leading to more frequent cholecystectomies [23]. The female gender has a most compelling association with gallstone disease, especially during the fertile years. Women are almost twice as likely as men to form stones; the gap narrows following menopause after which men begin to catch up [24]. The underlying mechanism is female sex hormones; parity, oral contraceptive use and estrogen replacement therapy are established risk factors for cholesterol gallstone formation [25]. In the present study it was observed that among 50 cases 30 cases (60%) were females and 20 cases (40%) were males and patients under the age group 51-60 years (40%) are mostly affected in gallstone diseases. According to this study 14 cases (28%) belongs to House wife and 45 cases (90%) were married and 5 cases (10%) were unmarried.

Obesity is an important risk factor for gallstone disease, more so for women than for men. It raises the risk of cholesterol gallstones by increasing biliary secretion of cholesterol, as a result of an increase in 3-hydroxy-3-mthylglutaryl coenzyme A (HMGCoA) reductase activity. Epidemiological studies have found that the lithogenic risk of obesity is strongest in young women, and that slimness protects against

cholelithiasis [26]. In the present investigation it was observed the most prevalence of the disease with over weight (80%), 12 % with normal BMI and 8% with obese.

This preponderance persists to a lesser extent into the postmenopausal period, but the sex difference narrows with increasing age. Increased levels of the hormone estrogen, as a result of pregnancy or hormone therapy, or the use of combined (estrogen-containing) forms of hormonal contraception, may increase cholesterol levels in bile and also decrease gallbladder movement, resulting in gallstone formation [27].

People with diabetes generally have high levels of fatty acids called triglycerides. These fatty acids may increase the risk of gallstones. Gallbladder function is impaired in the presence of diabetic neuropathy, and regulation of hyperglycemia with insulin seems to raise the lithogenic index [28]. High incidence of cases 68% was noted in irregular diet timing and the disease occurred to the people who consumed non-veg weekly once 71% were noted. The patients who consumed chicken meat had high incidence 60 % were noted. 20 cases (40%) were noted in no fasting category and,14 cases (70%) were noted under weekly once fasting category. 18 cases (36%) were comes under no morbidities. 10 cases (20%) were noted in diabetes mellitus. 6 cases (12%) came under both diabetes mellitus and hypertension. 3 cases (6%) were noted in both obesity and dyslipidaemia. 9 cases (18%) were noted as hypertension and 1 case (2%) was noted in typhoid fever.

A lack of melatonin could significantly contribute to gallbladder stones, as melatonin inhibits cholesterol secretion from the gallbladder, enhances the conversion of cholesterol to bile, and is an antioxidant, which is able to reduce oxidative stress to the gallbladder [29].The main determinant for gallstone formation in patients with cirrhosis of the liver appears to be the severity of liver disease. Advanced liver cirrhosis indicates a long duration of the disease. In the present study it was noted that 37 cases (74%) were noted in Non-alcohol consumption and 13 cases (26%) were noted with alcohol consumption. The incidence of daily alcohol consumption was noted about 54%. In smoking category 10 cases (20%) were noted in smoking habit and current smokers affected in 4 cases (40%), chain smokers were noted in 1 case (10%), previous smoker affected in 3 cases (30%) and

occasional smoker affected in 2 cases (20%). In physical exercise category, patients were affected with physical exercise was about 32 % in 16 cases.

5.Conclusion

Considering the higher level of incidence and morbidity gall stone disease requires systematic therapeutic and precautionary measures in its management. Apart from gender difference other comorbid condition like diabetes and sedentary lifestyle have greater influence on disease prevalence, hence prevention is better than cure as a synonym of this with proper diet, exercise and clean habit the occurrence of GSD will be greatly minimized.

Acknowledgement

6. References

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Table 1: Frequencies and Percentages of demographic characteristics and Descriptive analysis of studied sample risk factors (N=50)

Variables	Groups	Frequencies	Percentage
Gender	Male	20	40
	Female	30	60
Age Groups	18-30	10	20
	31-40	9	18
	41-50	11	22
	51-60	20	40
Occupation	Engineer	2	4
	Driver	2	4
	Farmer	2	4
	Professor	8	16
	Cooley	9	18
	Business	13	26
	Housewife	14	28
Marital Status	Married	45	90
	Unmarried	5	10
Type of diet	Vegetarian	15	30
	Mixed-diet	35	70
Diet timing	Regular	16	32
	Irregular	34	68
Period of non-vegetarian taken (35)	Often	10	29
	Weekly once	25	71
Type of Meat (35)	Beef	2	6
	Fish	4	11
	Mutton	8	23
	Chicken	21	60
Fasting	Yes	20	40
	No	30	60
Fasting period (20)	Occasionally	1	5
	Customary Fasting	2	10
	Monthly Once	3	15
	Weekly Only	14	70
Alcohol Consumption	Yes	13	26
	No	37	74
Period of Alcohol Consumption (13)	Occasionally	1	8
	Weekly Once	5	38
	Daily	7	54
Smoking Habit	Yes	10	20
	No	40	80
Period of Smoking Habit (10)	Chain Smoker	1	10
	Occasionally	2	20
	Previous Smoker	3	30
	Current Smoker	4	40

Physical Exercise	Yes	16	32
	No	34	68
Period of Physical	Daily	15	94
Exercise (16)	Weekly Once	1	6
Comorbidities	None	18	36
	Diabetes Mellitus	10	20
	Hypertension	9	18
	Diabetes Mellitus &		
	Hypertension	6	12
	Obesity	3	6
	Dyslipidaemia	3	6
	Typhoid Fever	1	2
Parity (30)	Multiparous	19	63
	Primiparous	6	20
	Nulliparous	5	17
Estrogen Therapy (30)	Yes	2	7
	No	28	93
Birth Control Pills (30)	Yes	10	34
	No	20	66
Total Bilirubin	Normal	33	66
	Abnormal	17	34
SGOT	Normal	13	26
(Aspartate Transaminase)	Abnormal	37	74
SGPT	Normal	24	48
(Alanine Transaminase)	Abnormal	26	52
Alkaline Phosphatase	Normal	32	64
	Abnormal	18	36
Total Protein	Normal	47	94
	Abnormal	3	6
Albumin	Normal	50	100
	Abnormal	0	0
Globulin	Normal	27	54
	Abnormal	23	46
BMI	Normal (19-24)	6	12
	Overweight (25-29)	40	80
	Obese (above 30)	4	8

Table 2: Association between gallstone diseases and risk factors

Variables	Male	Female	Total	P-value
Occupation				
Housewife	0	14	14	
Farmer	2	0	2	
Professor	4	4	8	0.043

Business	6	7	13	
Cooley	4	5	9	
Driver	2	0	2	
Engineer	1	1	2	
Parity				
None	18	2	20	
Nulliparous	0	5	5	<0.001**
Primiparous	0	6	6	
Multiparous	0	19	19	
Birth Control Pills				
Yes	0	10	10	0.004
No	20	20	40	
Type of meat	**Vegetarian**	**Mixed diet**		
None	12	0	12	
Mutton	0	8	8	
Beef	0	2	2	<0.001*
Chicken	0	21	21	
Fish	0	7	7	