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Studies on the Chemical Composition and Presentation of Gallstones in Relation to Sex and Age among Human Population of Multan, Pakistan

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Abstract: The present study was carried out to investigate chemical composition of gallstones and their presentation in patients of different age groups of human population in Multan, Pakistan for a period of 18 months from August 2001 to January 2003. Gallstones were diagnosed by ultrasound and ultra sonography specifically in gallbladder and in bile duct. After cholecystectomy gallstones were washed, dried and analyzed by infrared spectroscopic and chemical method for various bio-chemical components. Of the 303 cases of gallstones, 274 (90.42%) were in gall bladder and 29 (9.57%) were in the bile duct. The predominant symptoms associated with gallstones were pain in hypochondrium, 164 (54.12%), vomiting 54 (17.82%), nausea 30 (9.90%), fever 38 (12.54%) and fatty food 17 (5.61%). According to the chemical composition of the gallstones, most of the stones examined in this study were of cholesterol 86 (28.30%), calcium oxalate 53 (17.40%), calcium phosphate 21 (6.90%), pure uric acid 31 (10.30%), pure bile 55 (18.40%) carbonate + magnesium 33 (10.80%) and others 24 (7.90%) were of mixed lithiasis. Of these cases the incidence of formation of cholesterol stone, was maximum in all age groups of both sexes.

Key words: Chemical composition, gallstones, sex, age, population

INTRODUCTION

Cholelithiasis or formation of gallstones are one of the most painful diseases which affect human and are an important cause of morbidity in developed countries. In USA, for example, 20% of the women and 5% of the men between the ages of 50 and 65 have gallstones^[1]. It affects approximately 15% of the total population in UK^[2]. All the hepatic cells continually form a small amount of secretion called bile. This is secreted into the minute bile canaliculi that lie between the hepatic cells in the hepatic plates and the bile then flows peripherally toward the interlobular septa where the canaliculi empty into terminal bile ducts, then into progressively larger ducts, finally reaching the hepatic duct and common bile duct from which the bile either empties directly into the duodenum or is diverted through the cystic duct into the gall bladder^[3]. The bile secreted continually by the liver cells is normally stored in the gall bladder until needed in the duodenum. The total secretion of bile each day is some 700 to 1200 ml and the maximum volume of the gall bladder is only 30 to 60 ml. Nevertheless, as much as 12 h bile secretion can be stored in the gallbladder because water, sodium, chloride and most other small electrolytes are continually absorbed by

the gall bladder mucosa, concentrating the other bile constituents, including the bile salts, cholesterol, lecithin and bilirubin. Most of this absorption is caused by active transport of sodium through the gallbladder epithelium. Bile is normally concentrated about five fold, but it can be concentrated up to a maximum of 12-18 fold^[3]. Bile salts are formed in the hepatic cells from cholesterol and in the process of secreting the bile salts about one tenth as much cholesterol is also secreted into the bile. This amounts to a total of 1-2 g/day. No specific function is known for the cholesterol in the bile, but it is presumed that it is simply a byproduct of bile salt formation and secretion. Inflammation of the gallbladder epithelium often results from low-grade chronic infection; this changes the absorptive characteristics of the gallbladder mucosa, sometimes allowing excessive absorption of water, bile salts, or other substances that are necessary to keep the cholesterol in solution. As a result, cholesterol begins to precipitate, usually forming many small crystals of cholesterol on the surface of the inflamed mucosa. These in turn, act, as nuclei for further precipitation of cholesterol and the crystals grow larger and larger. Occasionally tremendous numbers of sand like stones develop, but much more frequently these coalesce to form a few large

stones, or even a single stone that fills the entire gall bladder. Gall stone disease is quite common in Pakistan^[4]. The diagnostic of all stones and their complications are usually made by ultrasonography or oral cholecystography. Investigations like computerized tomography, HIDA scan, Percutaneous transhepatic cholangiography and endoscopic retrograde choleangiopancreatography are required rarely. Ultrasound can show biliary calculi or sludge, dilatation of the biliary tree and carcinoma of the pancreas. It can also show the thickness of the wall of gallbladder^[4]. Gallstones are classified into two groups i.e cholesterol gallstones and pigment stones. The distinction can be made visually, bio-chemically and often radio-logically^[2]. Gallstones are formed as a result of many disorders and super saturation^[5]. The dietary cholesterol overloads the super saturation of cholesterol in bile, which results in subsequent cholesterol precipitation and stone formation. The over production of cholesterol by the liver is the major metabolic precedent of cholesterol gallstones and this may occur because of obesity, drugs and other factors^[5]. The purpose of the present study was to assess the chemical composition and presentation of gallstones in human population of Multan. Ancillary purpose of the research was to find out the relationship of gallstones with age and sex. This study will provide us with the answers related to nature and causes of gallstones and their possible preventions.

MATERIALS AND METHODS

The present study was carried out to assess the chemical composition and presentation of gallstones in relation to sex and age among human population of Multan, Pakistan for a period of 18 months from August 2001 to January 2003. The present study was based on the data of the patients (n=303) admitted in surgical units of Nishtar Hospital Multan. Two hundred twenty nine males and 74 females of different age groups were analyzed. The male population was divided into three age groups i.e. old male (age above 50 years), mature male (age 13 to 50 years) and young male (age below 13 years). The female population was also divided into similar three groups. Efforts were made to include samples of all those persons who were willing to cooperate in carrying out for the purpose of present study. Ultrasound of the liver and gallbladder was performed after over night fasting. The findings of ultrasound were studied and recorded. After the operation each stone was carried to Khan Diagnostic Laboratory where they were physically and bio-chemically analyzed by infrared spectroscopy and wet chemical analysis. Infrared spectroscopy is an extremely powerful

analytical technique for both qualitative and quantitative analysis. The infrared spectrum of unknown substance is interpreted by the use of specific light frequencies. The samples were washed with deionized water and dried in air. The I.R. spectrums of all samples were recorded. The standard spectrums of calcium, magnesium, phosphate and oxalate were also recorded. In wet chemical analysis method, the stone powder was obtained by pulverizing the small stones in an agate mortar. Stone powders were qualitatively analyzed for the presence of various substances by treating the powder with the chemical agents provided by the chemical kit (Merck) for the diagnosis of various types of chemical stones. The chemical composition and physical existence of the stones were then recorded and statistically analyzed^[6].

RESULTS

The present study revealed that tendency of single stone formation was higher 181 (59.73%) as compared to double 33 (10.89%) or multiple stones 89 (29.37%) in all age groups of both sexes (Table 1). The data further suggested that occurrence of stones is maximum 274 (90.42%) in gall bladder and 29 (9.57%) in bile duct (Table 2). The results showed that the tendency of formation of oval shaped stones 112 (37%) was highest. The percentage of rounded stones 77 (25.41%), spindle shaped stones 45 (14.85%), granular 30 (9.90%) and almond shaped stones were 39 (12.84%) (Table 3).

The results suggested that tendency of formation of hard stones 284 (93.72%) was greater than soft stones 19 (6.27%) in all age groups of both sexes (Table 4).

According to data brown stones were highest in percentage 118 (38.94%) then yellow colored 36 (11.88%), clay 43 (14.19%) gray 44 (14.50%) and blackish 62 (20.46%) (Table 5). According to chemical composition

Table 1: Gallstone patients with single, double and multiple stones

Types	Age	Sex	N	Single	Double	Multiple
Old	>50	M	49	27	6	16
Mature	13-50	M	125	75	15	35
Young	<13	M	55	31	07	17
Old	>50	Fe	14	12	0	2
Mature	13-50	Fe	51	27	5	19
Young	<13	Fe	09	9	0	0
Total			303	181	33	89
% Age				59.73%	10.89%	29.37%

Table 2: Patients with occurrence of gallstones in gall bladder and bile duct.

Types	Age	Sex	N	Gall bladder	Bile duct
Old	>50	M	49	42	7
Mature	13-50	M	125	119	6
Young	<13	M	55	46	9
Old	>50	Fe	14	12	2
Mature	13-50	Fe	51	47	4
Young	<13	Fe	09	8	1
Total			303	274	29
% Age				90.42%	9.57%

Table 3: Presentation of different shapes of gallstones in patients of all age groups of both sexes

Types	Age	Sex	N	Oval	Spindle	Rounded	Granuler	Almond
Old	>50	M	49	19	6	18	4	2
Mature	13-50	M	125	47	18	26	16	18
Young	<13	M	55	21	6	14	1	13
Old	>50	Fe	14	6	4	1	1	2
Mature	13-50	Fe	51	18	11	17	2	3
Young	<13	Fe	09	1	0	1	6	1
Total			303	112	45	77	30	39
% Age				37%	14.85%	25.41%	9.90%	12.84%

Table 4: Occurrence of hard and soft gallstones in patients of all age groups of both sexes

Types	Age	Sex	N	Hard	Soft
Old	>50	M	49	43	6
Mature	13-50	M	125	119	6
Young	<13	M	55	54	1
Old	>50	Fe	14	13	1
Mature	13-50	Fe	51	47	4
Young	<13	Fe	09	08	1
Total			303	284	19
% Age				93.72%	6.27%

Table 5: Presentation of different colors of gallstones in patients of all age groups of both sexes

Types	Age	Sex	N	Yellow	Clay	Brown	Gray	Blackish
Old	> 50	M	49	7	12	13	9	8
Mature	13 -50	M	125	15	17	44	22	27
Young	< 13	M	55	7	8	23	6	11
Old	> 50	Fe	14	1	1	8	1	3
Mature	13 -50	Fe	51	5	4	25	5	12
Young	< 13	Fe	09	1	1	5	1	1
Total			303	36	43	118	44	62
% Age				11.88%	14.19%	38.94%	14.5%	20.46%

Table 6: Chemical analysis of urinary stones in patients of all age groups of both sexes

Types	Age	Sex	N	Chol 100%	Calcium Oxalate 100%	Calcium Phosphat. 100%	Uric Acid 100%	Bile 100%	Carbonate + Magnesium	Mix
Old	>50	M	49	11	12	2	6	7	5	6
Mature	13-50	M	125	31	18	11	17	21	15	12
Young	<13	M	55	15	12	2	3	16	5	2
Old	>50	Fe	14	5	2	1	3	1	2	0
Mature	13-50	Fe	51	19	6	5	1	10	6	4
Young	<13	Fe	09	5	3	0	1	0	0	0
Total			303	86	53	21	31	55	33	24
% Age				28.3%	17.4%	6.9%	10.3%	18.4%	10.8%	7.9%

Table 7: Presentation of associated symptoms of gall stones In patients of all age groups of both sexes

Types	Age	Sex	N	Pain in hypochondrium	Vomiting	Nausea	Fever	Fatty food
Old	>50	M	49	28	8	6	4	3
Mature	13-50	M	125	86	15	6	15	3
Young	<13	M	55	19	11	7	10	8
Old	>50	Fe	14	7	2	2	2	1
Mature	13-50	Fe	51	19	17	8	6	1
Young	<13	Fe	09	5	1	1	1	1
Total			303	164	54	30	38	17
% Age				54.12%	17.82%	9.90%	12.54%	5.61%

the highest percentage of the stones was pure cholesterol stones 86 (28.30%) followed by bile stones 55 (18.40%), pure calcium oxalate 53 (17.40%), Carbonate and Magnesium stones 33 (10.80%), pure Uric acid 31 (10.30%), pure Calcium Phosphate, 21 (6.90%) and others 24 (7.90%) were of mixed lithiasis (Table 6). The predominant symptoms associated with gallstones were pain in hypochondrium, 164 (54.12%), vomiting 54

(17.83%), nausea 30 (9.90%), fever 38 (12.54%) and fatty food 17 (5.61%).

DISCUSSION

As Pakistan is situated in the stone kit, so Cholelithiasis or formation of gallstones is responsible for considerable morbidity. The present study revealed that

tendency of single stone formation was higher as compared to double or multiple stones in all age groups of both sexes. The data further suggested that occurrence of stones is maximum in gall bladder and as compared to in bile duct. The results showed that the tendency of formation of oval shaped stones was highest as compared to the percentage of rounded, spindle shaped granular and almond shaped stones. The results suggested that tendency of formation of hard stones was greater than soft stones in all age groups of both sexes. According to data brown stones were highest in percentage then yellow colored, clay, gray and blackish. According to chemical composition the highest percentage of the stones was pure Cholesterol stones followed by Bile stones, pure Calcium Oxalate, Carbonate and Magnesium stones, pure Uric acid Calcium Phosphate and others were of mixed lithiasis. The predominant symptoms associated with gallstones were pain in hypochondrium, vomiting, nausea, fever and fatty food. The results of the present study revealed that among the reported operated cases gallstone is most prevalent in mature patients of an age group 13-50 years. The most important clinical feature of Cholelithiasis is recurrent abdominal pain, which is often colicky and localized to the right upper quadrant. An older child may have intolerance for fatty foods. Acute Cholecystitis may be the first manifestation, with fever, pain in the right upper quadrant and often a palpable mass. Pain may radiate to an area just below the right scapula. A pain roentgenogram of the abdomen may reveal opaque calculi, but radiolucent (cholesterol) stones are not visualized. Accordingly, ultrasonography is the method of choice for gallstone detection. Laparoscopic cholecystectomy is commonly performed in symptomatic children with cholelithiasis. Common bile duct stones are unusual in children occurring in 2-6% of cases with cholelithiasis, often in association with obstructive jaundice and pancreatitis^[7]. Cholelithiasis is relatively rare in children, occurring more commonly in patients with various predisposing disorders. Gallstones, composed of a mixture of cholesterol, bile pigment, calcium and inorganic matrix, are common.

Cholelithiasis, i.e, the presence of gallstones, is a common condition. It's incidence increases with age, so that in the USA, for example, 20% of the women and 5% of the men between the ages of 50 and 65 years have gall stones. In the USA and Europe, 85% of the stones are cholesterol stones^[1]. Bilirubin is an orange pigment produced by the break down of haem in the macrophages. It is carried in the plasma bound to albumin and taken up into the hepatocytes by facilitated diffusion. Within the cell, bile acid binds to a protein known as Y protein and is then conjugated with glucuronic acid. It is secreted by

active transport into the canaliculus and excreted with the bile into the duodenum. Bilirubin is degraded by colonic bacteria to urobilinogen, some of which is absorbed into the blood; most is re-excreted in the bile but some is excreted in the urine. Failure of the body to excrete the bilirubin produced by red cell destruction (haemolysis) causes jaundice. Jaundice can result from excessive haemolysis which overwhelms the livers excretory capacity, or from damage to hepatocytes (hepatocellular jaundice) or from blockage of the bile ducts (obstructive jaundice)^[8]. Large sized stone formation is the result of enhanced attachment of crystals to the surface of cells and is reduced by the inhibitors of crystal growth and aggregation. These stone may be of different shapes and sizes. The data of the present study shows that stones are of different colors. It is because of the fact; maximum stones contain Calcium and Uric acid. Calcium stones are white in color and their surface is rough. Uric acid and urate stones are yellow or brown in color and are smooth and hard. Uric acid stones form when there is too much Uric acid in diet. In mix lithiasis traces of Cystine are also observed. But Cystine stones are rare. Cystine is one of the building blocks that make up muscles, nerves and other parts of the body. This means that small changes in Oxalate concentration have much larger effects on Calcium Oxalate crystallization than larger changes in Calcium concentration.

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