

EVALUATION OF RISK FACTORS OF GALLSTONE DEVELOPMENT.

Zahoor Hussain Bhellar¹, Zulfiqar Ali Shar¹, Sirajuddin², Abu Baker³, Ali Gohar Bozdar⁴, Azad Ali Lashari⁴.

ABSTRACT

INTRODUCTION: Certain factors encourage the development of stones in gall bladder. These factors are: lack of exercise, dyslipidemia, consuming poor diets (e. g. starchy foods) ultimately activates the liver for cholesterol formation, bile saturation. Gall stones are one of the common disorders all over the world and women are more affected than men. It is curable depending upon the condition of the disease. **OBJECTIVE:** risk factors of gallstone development. **METHODOLOGY:** This is a descriptive quantitative study. The risk factors of gallstone development were assessed and evaluated at Department of Surgery, Khairpur Medical college Hospital Khairpur Mir's, a public sector hospital of Sind (Pakistan). The inclusion of patients was done for a six months period from May 2019 to October 2019. A total of 119 patients were included during the study period. **RESULT:** 64.7% patients were of cholesterol gallstones while 35.3% patients were of pigment gallstones. More male respondents were having cholesterol gallstones while all women were having pigment gallstones. **CONCLUSION:** The study confirms that earlier findings of other authors that gender (female), age (40 – 49 years), BMI 25 and above, sedentary lifestyle and high cholesterol food were the prominent factors for causing gallstones.

KEY WORDS: Cholesterol Gallstone, Pigment Gallstone, BMI, Lifestyle, Sedentary Lifestyle, Hypercholesterolemia

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INTRODUCTION

When the digestive fluids deposited in the gallbladder are hardened, gallstones are formed. It blocks the emptying of gallbladder. The symptoms include pain and fever. The pear shaped gall bladder is an important part of the biliary system. It stores bile and secretes it into the small intestine upon requirement. The other function of gall bladder includes regulating the equal pressure in the biliary system to assist in maintaining the bile pH¹.

Several risk factors encourage the formation of gall stone in the gall bladder. For instance, the lack of the components of digestive enzymes encourage the formation of crystals in gall bladder, these crystals may be due to high cholesterol level, hyperbilirubinemia, in liver diseases, blood disorders can induce excessive bilirubinemia and cause the

formation of dark and black stones in the gall bladder².

Further to this, obesity, a sedentary lifestyle, or poor diet consumption in terms of taking high fat diets are more likely to develop cholesterol related stones in the gall bladder. Several types of medications are associated with the formation of gall stones. The other common condition of the gall stone formation is the concentration of bile because of the fullness of gall bladder. Improper secretion of bile from gall bladder hurts the gall bladder in terms of the stone formation inside the bladder³.

The common symptoms by which the presence of gall stone is identified are pain in the upper abdominal region, nausea, vomiting, the changes in urine and stool are also reported, the dark-colored urine, the light colored stool are reported due to the presence of gall stone. The test that confirms

the presence of gall stone is the high gamma glutryl transferase (GGT) level, normal to high alkaline phosphatase (ALP) level. Studies suggest that least number of patients reported for the normal alkaline phosphatase level, high bilirubin level, if 10 or more times higher of cholesterol level, then gall stone is more likely to develop due to cholesterol and is called cholestasis⁴. The other diagnostic approach includes ultrasound screening such as abdominal ultrasound, endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiopancreatography, etc⁵.

Further to this, in this advanced era, the gall stone is treated differently depending on the condition and severity of the disease. The gall bladder when saturated or filled with stones, it is surgically removed. This has also been found by several studies that lack of gallbladder does not cause negative effects on the patient's metabolism. Few patients need post-therapy regarding releasing the complication of the negative consequences of lacking gall bladder⁶.

The other mode of therapy is laparoscopy, under anesthesia, the hole is created at the right upper quadrant of the abdomen where gall bladder is present, three to four incisions are created by which the endoscopy needle, laser needles are passed to pass laser beam of light, the stone is crushed and is sucked which is the part of the laparoscopy equipment. In addition to this, depending on the condition of disease, the non-surgical approach is usually adopted primarily to release the patient's suffering. Several medicines like ursodiol, chenodiol, and many other bile liquefying pills are available that dilute the bile or assist in solubilizing the stone to release from the body. Usually, this is noticed that gall stone at the primary stage is usually recovered by certain medications⁷.

Risk Factors of the development of Gall stones

Obesity:

Obesity or high BMI is one of the major causes encouraging gall stone development. Several peered articles reported that high abdominal fat causes low mobility and bile stasis, this irregularity causes the pressure inequilibrium in the biliary region by which the stones are formed in gall bladder. Women are more likely to develop gall stones. In pregnancy, the ALP (alkaline aminotransferase) is usually high and the weight gain by women affects the hepatobiliary function eventually develops the stones in the gall bladder. One out of ten

women is affected by gall stone after giving birth to their babies. The gall stone formation mechanism speeds up by hypercholesterolemia⁸.

In women, the estrogen level is generally high in pregnancy and the case of post-pregnancy of estrogen level is more likely to cause gall stone formation. The reason documented by several author is: estrogen is produced by adipocytes which enhances the mechanism of cholesterol efflux in the liver; the elevated hepatobiliary function regarding cholesterol efflux causes the formation of cholestasis. Obesity or high BMI (body mass index) affects insulin mechanism and encourages the formation of lithogenic bile via hyper activating the lipolysis mechanism in the liver which causes gall bladder fullness condition. This eventually causes the cholesterol precipitation in the form of gall stone⁹.

Hypercholesterolemia:

This is traditionally considered that a high serum level of cholesterol, LDL, and low serum level of HDL enhances the secretion of cholesterol in bile. In addition to this, cholesterol in bile dense the secretion and alter the pH in terms of acidity. This irregularity eventually causes the precipitation of bile in the form of stone formation which ultimately influences other intestinal mechanisms. Moreover, the stone formation also influences the hepatobiliary function for bile formation due to damage of liver cells taking part in synthesizing bile acids¹⁰.

The biliary tract infection accentuates stone formation in the gall bladder. This is considered that bacterial infection forms brownstones in gall bladder due to bacterial over activation mechanism of hydrolysis of conjugated bilirubin into a less soluble form which is unconjugated. Further to this, calcium salt content is also high in a bacterial infection leading to gall stones formation. Several articles reported that calcium salts are the main source of the super saturation and also acidifying bile leading stone formation inside the gall bladder¹¹.

Bowel Transit:

Besides the liver and gall bladder, the intestine is another main organ involved in the development of gall stones. The gall bladder and small intestine take part in the enterohepatic movement of bile salts and their reflux in the liver. The patient suffering from gall stone usually has a prolonged transit time. Impaired intestinal mobility is more likely to cause gall stone formation.

The deoxycholate, a secondary bile salt is mostly formed by bacterial fermentation. Due to the prolonged transit time of intestine, the deoxycholic acid is formed with more residual salt in the intestine and has the opposing effect in term of deposition of this salt in the gall bladder¹².

Postprandial Gall Bladder Motility:

Under normal condition, the gall bladder is 70 to 80% empty through stimulating the cholecystokinin (CCK) hormone present in the duodenal wall. The poor emptying either due to physical inactivity, high consumption of high caloric diet, or a very low caloric diet lacking the essential elements like calcium, magnesium, or other elements encouraging the irregular fashion of gall bladder emptying and cause nucleation of bile salts which is another form of stone in the gall bladder¹³.

Further to this, refilling of gall bladder lacking essential components and proteins or due high level of cholesterol cause the thickening of secretion eventually affect the intestinal activity either in the form of enhancing the transit time of intestine or either cause the nucleation of bile salts in the gall bladder. This condition is highly encouraged by taking a heavy meal in dinner or taking a meal few minutes before going to night sleep. Further to this, this mechanism is also enhanced by hyperinsulinemia which affects the liver signaling for cholesterol metabolism. The poor diet and overactive liver function for cholesterol metabolism are reported more for the gall stone formation¹⁴.

Methodology

This is a descriptive quantitative study. The risk factors of gallstone development were assessed and evaluated at Department of Surgery, Khairpur Medical college Hospital Khairpur Mir's, a public sector hospital of Sind (Pakistan). The patients were screened at the Surgical OPD and then referred to the radiology department where the presence of gallstones were confirmed through ultrasound examination. The sampling was done on the basis of consecutive cases of gallstones in the surgical OPD of the hospital. The inclusion of patients was done for a six months period from May 2019 to October

2019. A total of 119 patients were included during the study period.

Medical options were not considered and all patients were treated with surgical procedure.

However, since the study is limited to the evaluation of risk factors the treatment option has not been discussed in detail.

RESULT

The value of Cronback's Alpha .874 means that 87.4% of the independent variables used to define the dependent variable, define it well.

64.7% patients were of cholesterol gallstones while 35.3% patients were of pigment gallstones. More male respondents were having cholesterol gallstones while all women were having pigment gallstones.

Age wise 69.7% patients were of 40 – 49 years while about 18.5% 50 – 59 years. In cross tabulation with BMI, 48.7% were having a BMI of 25 – 29.9 while 51.3% were having a BMI of 30 and above. In terms of lifestyle 63% patients were having sedentary lifestyle while 17.6% were having urban lifestyle. In terms of eating behavior 87.4% patients were having fast food or fatty food. In terms of serum level of cholesterol 68.1% were having a high cholesterol level (240 mg/dL and above) while 39.1% were having borderline cholesterol level (between 200 and 239 mg/dL). **TABLE 2: PATIENTS OF GALL STONES * GENDER Cross tabulation**

TABLE 3: PATIENTS OF GALL STONES * AGE Cross tabulation

TABLE 4: PATIENTS OF GALL STONES * BMI Cross tabulation

TABLE 5: PATIENTS OF GALL STONES * LIFESTYLE Cross tabulation

TABLE 6: PATIENTS OF GALL STONES * EATING BEHAVIOR Cross tabulation

TABLE 7: PATIENTS OF GALL STONES * HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL) Cross tabulation

Table 1: Reliability Statistics	
ronbach's Alpha	N of Items
.874	7

TABLE 2: PATIENTS OF GALL STONES * GENDER Cross tabulation							
			GENDER		Total	Sig value	
			MALE	FEMALE			
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	47	30	77		
		% within PATIENTS OF GALL STONES	61.0%	39.0%	100.0%		
		% within GENDER	100.0%	41.7%	64.7%		
	PIGMENT GALLSTONES	Count	0	42	42		
		% within PATIENTS OF GALL STONES	0.0%	100.0%	100.0%		
		% within GENDER	0.0%	58.3%	35.3%		
Total		Count	47	72	119	0.000	
		% within PATIENTS OF GALL STONES	39.5%	60.5%	100.0%		
		% within GENDER	100.0%	100.0%	100.0%		

TABLE 3: PATIENTS OF GALL STONES * AGE Cross tabulation								
			AGE				Total	Sig value
			30 – 39 YEARS	40 – 49 YEARS	50 – 59 YEARS	60 YEARS AND ABOVE		
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	3	74	0	0	77	
		% within PATIENTS OF GALL STONES	3.9%	96.1%	0.0%	0.0%	100.0%	
		% within AGE	100.0%	89.2%	0.0%	0.0%	64.7%	
	PIGMENT GALLSTONES	Count	0	9	22	11	42	
		% within PATIENTS OF GALL STONES	0.0%	21.4%	52.4%	26.2%	100.0%	
		% within AGE	0.0%	10.8%	100.0%	100.0%	35.3%	
Total		Count	3	83	22	11	119	0.000
		% within PATIENTS OF GALL STONES	2.5%	69.7%	18.5%	9.2%	100.0%	
		% within AGE	100.0%	100.0%	100.0%	100.0%	100.0%	

TABLE 4: PATIENTS OF GALL STONES * BMI Cross tabulation							
			BMI		Total	Sig value	
			25 – 29.9 (OVER WEIGHT)	30 AND ABOVE (OBESE)			
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	58	19	77		
		% within PATIENTS OF GALL STONES	75.3%	24.7%	100.0%		
		% within BMI	100.0%	31.1%	64.7%		
	PIGMENT GALLSTONES	Count	0	42	42		
		% within PATIENTS OF GALL STONES	0.0%	100.0%	100.0%		
		% within BMI	0.0%	68.9%	35.3%		
Total		Count	58	61	119	0.000	
		% within PATIENTS OF GALL STONES	48.7%	51.3%	100.0%		
		% within BMI	100.0%	100.0%	100.0%		

TABLE 5: PATIENTS OF GALL STONES * LIFESTYLE Cross tabulation								
			LIFESTYLE			Total		Sig value
			SEDENTAR LIFESTYLE	BOHEMIAN LIFESTYLE	RURAL LIFE STYLE	URBAN LIFESTYLE		
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	75	2	0	0	77	0.000
		% within PATIENTS OF GALL STONES	97.4%	2.6%	0.0%	0.0%	100.0%	
		% within LIFESTYLE	100.0%	15.4%	0.0%	0.0%	64.7%	
	IPIGMENT GALLSTONES	Count	0	11	10	21	42	
		% within PATIENTS OF GALL STONES	0.0%	26.2%	23.8%	50.0%	100.0%	
		% within LIFESTYLE	0.0%	84.6%	100.0%	100.0%	35.3%	
Total		Count	75	13	10	21	119	
		% within PATIENTS OF GALL STONES	63.0%	10.9%	8.4%	17.6%	100.0%	
		% within LIFESTYLE	100.0%	100.0%	100.0%	100.0%	100.0%	

TABLE 6: PATIENTS OF GALL STONES * EATING BEHAVIOR Cross tabulation							
			EATING BEHAVIOR			Total	Sig value
			DIETING / FASTING	VEGETARIAN	FAST FOOD / FATTY FOOD		
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	11	4	62	77	0.000
		% within PATIENTS OF GALL STONES	14.3%	5.2%	80.5%	100.0%	
		% within EATING BEHAVIOR	100.0%	100.0%	59.6%	64.7%	
	IPIGMENT GALLSTONES	Count	0	0	42	42	
		% within PATIENTS OF GALL STONES	0.0%	0.0%	100.0%	100.0%	
		% within EATING BEHAVIOR	0.0%	0.0%	40.4%	35.3%	
Total		Count	11	4	104	119	
		% within PATIENTS OF GALL STONES	9.2%	3.4%	87.4%	100.0%	
		% within EATING BEHAVIOR	100.0%	100.0%	100.0%	100.0%	

TABLE 7: PATIENTS OF GALL STONES * HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL) Cross tabulation							
			HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL)		Total	Sig value	
			ii) BETWEEN 200 AND 239 MG/DL (BORDERLINE HIGH)	240 MG/DL AND ABOVE (HIGH).			
PATIENTS OF GALL STONES	CHOLESTEROL GALLSTONES	Count	38	39	77	0.009	
		% within PATIENTS OF GALL STONES	49.4%	50.6%	100.0%		
		% within HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL)	100.0%	48.1%	64.7%		
	IPIGMENT GALLSTONES	Count	0	42	42		
		% within PATIENTS OF GALL STONES	0.0%	100.0%	100.0%		
		% within HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL)	0.0%	51.9%	35.3%		
Total		Count	38	81	119		
		% within PATIENTS OF GALL STONES	31.9%	68.1%	100.0%		
		% within HYPERCHOLESTEROLEMIA (HIGH SERUM LEVEL OF CHOLESTEROL)	100.0%	100.0%	100.0%		

DISCUSSION

In our study we found patients having cholesterol gallstones as well as pigment gallstones. More male respondents were having cholesterol gallstones while all women were having pigment gallstones. Thiazide diuretics are given to treat hypertension and several cardiovascular diseases with the main aim of enhancing biliary cholesterol saturation. It was observed that patient's do develop complications in terms of gall stone formation. To enhance the lithogenic property of bile a number of medicines are given¹⁵. The estrogen associated medicines cause the hyper secretion of cholesterol in bile which is more likely to cause increased intestinal transit time and develops pressure in bile reuptake. This disturbance eventually encourages the stone formation in the gall bladder.

In addition to this, the progesterone prevents acyl-coenzyme –A—acyltransferase delayed the cholesterol transformation into cholesteryl esters and induce the biliary sludge and eventually make bile more lithogenic. Other medicines like erythromycin or ampicillin, cyclosporine, anticoagulants, narcotics, anticholinergic medications are also reported to develop gall stones¹⁶. The findings of our study was that serum level of cholesterol 68.1% were having a high cholesterol level (240 mg/dL and above) while 39.1% were having borderline cholesterol level (between 200 and 239 mg/dL) due to the impact of medicines they were taking.

The high-fat diet or diet lacking fiber is more likely to cause gall stone formation. The high consumption of animal proteins, saturated fats, high carbohydrate diet, excessive alcohol consumption, inadequate water intake etc. are common elements that hurt gall bladder in the formation of gallstone¹⁷. This finding has been confirmed in our findings as well. It has also been reported that vegetarian people are less likely to develop gallstones because plant based diets are rich in fiber, sterol compounds that block cholesterol absorption through the portal system. This causes the emulsification of fats and dietary fibers to take cholesterol out of the body. This finding correlates with our findings. Further to this, the starchy or high sugar content possessing diets increases the risk of gallstone formation by 60%. To clear sugar from circulation, an excessive amount of insulin is required which eventually enhances the liver mechanism of cholesterol formation and concentrated them into bile. The concentrated bile later precipitates in the

form of particles and is deposited in the gall bladder as stones¹⁸.

CONCLUSION

The risk factors were evaluated for this study. It was found that patients of 40 – 49 years were having high prevalence, the female risk factor has been proven correct whose incidence was found to be 60.5%. Age wise 40 – 49 years were found to be more vulnerable. In the risk factors BMI the overweight and obese were having almost equal prevalence (25 – 29.9 and 30 and above). Sedentary life style was found to be the most prominent factor (63%) for causing gallstones. In terms of eating behavior the study confirmed that fast food / fatty food is the most prominent factor (87.4%) for causing gallstones. High cholesterol food was another prominent factor for causing gallstones.

Through modifying the dietary pattern, like managing body weight, consuming more fiber-rich diets like fruits and vegetables and etc., more water intake, exercise, good quality sleep, taking no meal two hours before night sleep, avoid consuming alcohol, avoid company manufactured juices and other confectionary items, avoid consuming high carb diets like bakery items, fast foods and etc. animal proteins can prevent the human from developing such types of stone in the gall bladder. The people should get aware of how altering lifestyle can create a significant impact on their livings and also save money in terms of taking treatments to attain normal health.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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