Full Length Research Paper

Characteristics of endoscopic retrograde cholangiopancreatography (ERCP) patients and predictors of common bile duct (CBD) stones in a Tertiary Hospital, Saudi Arabia

Wael. A. Shahin[1,2]* and Hassan. A. Bokhary[1]

[1]Department of Medicine, Division of Gastroenterology, Alnoor Specialist Hospital, Makkah, Saudi Arabia.
[2]Department of Tropical Medicine, Benha Faculty of Medicine, Benha, Egypt.

Biliary disorders vary in different parts of the world. Study of endoscopic retrograde cholangiopancreatography (ERCP) cases gives an idea about the biliary disorders in the community. The aim of the study is to determine the characteristics of ERCP patients and predictors of common bile duct (CBD) stone in a tertiary hospital in Makkah, Saudi Arabia. This study was conducted on 135 patients admitted at Al Noor Specialist Hospital, Makkah, during the years 2009 and 2010. Patient demographics, presentation, liver function tests, comorbid conditions, ultrasound and ERCP findings were studied. The mean age of patients was 46.59 ± 17.6 yrs and female / male ratio was 1.56/1. Female patients were significantly younger, having more biliary colic (42.7 vs. 11.3%), biliary pancreatitis (11 vs. 3.8%), gall bladder stones (64.6 vs. 56.6%), history of cholecystectomy (12.2 vs. 5.7%) and less serum bilirubin (4.27± 3.95 vs. 9.73 ± 7.95), while male patients presented with obstructive jaundice more than female patients (84.9 vs. 46.3%). Pancreatico-biliary malignancy was found in jaundiced, diabetic patients older than 65 years. There was CBD stone in 56.3% of patients, CBD stones was significantly less in biliary pancreatitis patients (4 vs. 13.6%). Predictors of CBD stones were history of cholecystectomy, high alanine transaminase (ALT) and high alkaline phosphatase (ALP) serum levels. The sensitivity and specificity of abdominal ultrasound in detecting CBD stones were 69.5 and 88.1%. ERCP patients in Makkah are similar to patients in other areas of Saudi Arabia. No significant difference between Saudi and Non Saudi patients. Malignancy should be suspected in old age, diabetic, jaundiced patients. Biliary pancreatitis is more common in female patients with low incidence of CBD stones. Predictors of CBD stones are previous cholecystectomy, high ALT and high ALP serum levels. Abdominal ultrasound is still a good screening tool for CBD stones detection.

Key words: Endoscopic retrograde cholangiopancreatography (ERCP), common bile duct (CBD) stone predictors, Makkah, Saudi Arabia.

INTRODUCTION

Endoscopic retrograde cholangio-pancreatography (ERCP) was introduced in the 1970s as a tool for the diagnosis and treatment of biliary disorders. The success rate of ERCP reaches over 85% with a mortality of 0.5 to 3.7% and immediate severe morbidity of 2.5 to 11%

(Freeman et al.,1996; Topal et al., 2003). ERCP is most commonly performed to diagnose conditions of the pancreas or bile ducts, and gives an idea about biliary disorders in the community.

The prevalence of gallstone disease varies around the world; ultrasound studies revealed gallstone disease in about 10 to 15% of adult individuals in western countries and in 3 to 5% of African and Asian populations (Kratzer et al., 1999). In Saudi Arabia, gallstone disease was

---

*Corresponding author. E-mail: waelzaki1@hotmail.com.

virtually unheard of 50 years ago, but, with increasing affluence and a western type diet, gall stones became as common as in many western countries (Johnson, 2001). Nearly every year, 1 to 3% of people worldwide develop gallstones (Yusoff et al., 2003). About 60 to 80 % of gallstones are silent, giving no symptoms, and need no treatment (Sauerbruch and Baumgartner, 1991). Approximately, 10 to 20% of gallstone patients are found to have associated common bile duct common bile duct (CBD) stones at the time of diagnosis (Barbara et al., 1987; Ko and Lee, 2002). The natural history of CBD stones is unpredictable, varying from no symptoms to life-threatening conditions as suppurative cholangitis, which has a mortality of 13 to 88% if left untreated (Lai et al., 1992; Rosseland and Glomsaker, 2000).

Several diagnostic tools have been used to diagnose CBD stones; including serum liver biochemical tests (for example, serum bilirubin, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase), transabdominal ultrasound (US), computed tomography (CT) abdomen, magnetic resonance imaging, Endoscopic ultrasound (EUS) and ERCP (ASGE 2010). Abdominal US is frequently used in the diagnosis of gallbladder (GB) stones because of its high specificity, but is less sensitive in diagnosing CBD stones, especially if they do not cause dilatation of the bile duct (Caddy and Tham, 2006). The sensitivity of abdominal US in detecting CBD stones was reported to be 50% and a negative predictive value of 82% (Bose et al., 2000), while for CT, the sensitivity was 69 to 88% and the specificity was 83 to 97% (Anderson et al., 2008), and for magnetic resonance imaging the sensitivity was 88 to 100% and specificity was 72 to 97% (Scaffidi, 2009). The sensitivity and specificity of EUS varies between 89 to 94% and 94 to 95% respectively (Tse, 2008), also, it can diagnose microlithiasis (stones < 3 mm) (Edmundowicz et al., 1992). In patients with no history of jaundice or pancreatitis, normal liver function tests and normal sized common bile duct (≤ 5 mm), the risk of CBD stone is as low as 6% (Majeed, 1999).

CBD stones may pass spontaneously into the duodenum without causing symptoms or reside in the bile duct for a long time and still be asymptomatic (Metcalfe, 2004). Patients with symptomatic CBD stones could have a higher risk of developing a complication, studies have shown a risk of 25 to 50% of jaundice, cholangitis or pancreatitis if the stones were left untreated (Williams, 2008). Bile duct stones can also be formed in the absence of gallbladder stones (primary bile duct stones) which are more common in East Asian countries due to associated biliary parasitic infestation (Tazuma, 2006).

In this study, we tried to define the characteristics of patients referred for ERCP in a tertiary hospital in Makkah, Saudi Arabia as a representative of a developing country with an increasing affluence and western type of food. Also, we tried to define the predictors of CBD stones which are the cause of most of the morbidity and mortality of gall stone disease. This will give an idea about biliary and pancreatic disorders in this particular community and will improve the identification of patients who have CBD stones.

METHODS

Study site and population

This is a descriptive retrospective study conducted on 135 adult patients admitted because of biliary or pancreatic symptoms and referred for ERCP. The study was done at Al Noor Specialist Hospital, Makkah, Saudi Arabia during the years 2009 and 2010. Al Noor Specialist Hospital is a well-equipped, 600 beds tertiary hospital in Makkah.

Study design

All patients were investigated and prepared for ERCP; written consent was given after explanation of the procedure, benefits, possible complications and the alternatives. Data were implemented on the Hospital Information System (HIS) according to the disease coding system ICD-10 AM (International Classification of Disease-10, Australian Modification), version 2006. The clinical, laboratory, radiological and ERCP data were collected including: age, sex, nationality, mode of presentation, laboratory results, abdominal US and co-morbid conditions as diabetes mellitus and ERCP findings.

ERCP was done under conscious sedation using midazolam 2.5 mg as a pre-procedure medication and diazepam (0.1 to 0.2 mg/kg body weight) to keep the patient in comfort, a pulse oxymeter was connected to the patient during and after the procedure in recovery area. Olympus duodenoscope video-system TJF-240 was used. The contrast material was urografin (76%) plus 40 mg gentamicin. After CBD cannulation, sphincterotomy was performed when indicated using Boston Scientific Triple lumen Sphincterotome (5.5 F, 20 mm, Manufactured by: Boston Scientific, 780 Brookside Drive, Spencer IN 47460, USA.) CBD stones extraction was done using extraction balloon (Fusion Quattro Extraction Balloon, 6.6 F, Manufactured by: Wilson-Cook Medical Inc. 4900 Bethania Station Road, Winston-Salam NC, 27105, USA). If stones could not be extracted, an appropriate stent was inserted (OASIS one action stent introduction system with preloaded cotton-leung biliary stent different sizes. Manufactured by: Cook Ireland Limited, O'Halloran Road, National technology Park, Limerick, Ireland).

Statistical analysis

All data were entered and analyzed using Microsoft

Table 1. Age, presentation and LFTs comparison in male and female patients.

Parameter	All (135 pat)	Male(M) 53 (39.3%)	Female (F) 82 (60.7%)	P value
Age (yr) (Mean ± Std. Dev)	46.59 ±17.6 (17 – 85)	51.36 ±18.4 (17- 85)	42.37 ± 16.4 (20 – 77)	0.008*
Obstructive jaundice	83 (61.5%)	45 (84.9%)	38 (46.3%)	<0.05*
Biliary colic.	41(30.4%)	6(11.3%)	35 (42.7%)	<0.05*
Biliary pancreatitis	11 (8.1%)	2 (3.8%)	9 (11%)	<0.05*
GB stones	83 (61.5%)	30 (56.6%)	53 (64.6%)	>0.05
Cholecystectomy	13 (9.6%)	3 (5.7%)	10 (12.2%)	<0.05*
T. bilirubin (up to 1 mg/dl)	6.42 ± 6.41 (0.23 - 30.00)	9.73 ± 7.95 (0.23 - 30.00)	4.27± 3.95 (0.27 – 18.0)	<0.05*
ALT (up to 40 IU/dl)	188.97 ± 167.91(9 – 780)	159.86 ±143.23 (21- 589)	207.52 ± 180.3 (9 – 780)	>0.05
AST(up to 37 IU/dl)	147.70 ± 148.96 (17 – 822)	119.33 ±107.38 (20 – 618)	165.91± 168.5 (17 – 822)	>0.05
ALP (up to 100 IU/dl)	323.66 ± 219.43 (65 – 1092)	297.60 ±191.05 (67- 967)	342.91± 237.8 (65 – 1092)	>0.05

By logistic regression the only significant parameter is age (p value 0.012). LFTs: liver function tests. ALT: alanine aminotransferase. AST: aspartate aminotransferase. ALP= alkaline phosphatase. IU = International Unit. (*)= statistically significant difference.

Table 2. Age, presentation and LFTs comparison in Saudi and non Saudi patients.

Parameter (Mean ± standard deviation)	Saudi (89 patients, 65.9%)	Non saudi (46 patients, 34.1%)	P value
Age (yrs)	45.3 ±17.5	47.02 ±17.1	>0.05
Biliary colic (41 patients)	30(34%)	13(28%)	>0.05
Obstructive jaundice(83 pt)	53(60%)	28(61%)	>0.05
Biliary pancreatitis(11pt)	6(6%)	5(11%)	>0.05
T-bill (up to 1 mg/dl)	6.06 ± 6.4	6.8 ± 6.5	>0.05
D bill (up to 0.25mg/dl)	4.4 ± 4.9	5.1 ± 5.2	> 0.05
ALT(up to 40 IU/dl)	190.3 ±175	205.8 ±166.7	>0.05
AST(up to 37 IU/dl)	142.9 ±140.5	157.3 ±167.9	> 0.05
ALP (up to 100 IU/dl)	270.2 ±166.6	328.1 ± 226.2	> 0.05

Office Excel 2007 and SPSS statistics 17.0 program. The results were expressed as the mean ± standard deviation (SD) for quantitative variables and percentage for categorical variables. Categorical variables were compared using the Chi-square test and two-tailed Student's *t* test to compare two means, and Spearman's rank-order correlation coefficient for nonparametric correlations. Univariate analysis by using Pearson Chi square test was used to compare dichotomous or categorical variables. *P* values of 0.05 or less were considered statistically significant.

RESULTS

This study included 135 patients, females were more than males (ratio 1.56/1) and significantly younger. The mean age was 46.59 ± 17.6 yrs. Seven patients had Diabetes Mellitus (5.2%), five of them were female and 5 were Saudi and the mean age was 61.9 ± 8.6 yrs. Three

patients had pancreatico-biliary malignancy, the mean age was 68 ± 3.6 yrs and all of them were diabetic and jaundiced patients. Obstructive jaundice was the commonest presentation (61.5%) and it was significantly more common in males, while biliary colic (30.4%) and biliary pancreatitis (8.1%) were significantly more common in females. Serum bilirubin was significantly lower in females while liver function tests (LFTs) (ALT, AST and ALP) were higher in females but not reaching the significant level, by logistic regression analysis. The only significant parameter between males and females was age (p value 0.012) (Table 1). There was no significant difference between Saudi and Non Saudi patients as regards the age, presentation and LFTs (Table 2).

The causes of obstructive jaundice were CBD stones in 73 cases (88%), Mirizi syndrome (4 cases, 4.8%), CBD stricture (3 cases, 3.6%) and pancreatic and ampullary masses (3 cases, 3.6%).

Table 3 showed the correlation between CBD diameter

Table 3. Correlation between CBD diameter and patient's age, presentation and LFTs.

CBD Diameter	CBD < 8 mm	CBD 8-12 mm	CBD13-18 mm	CBD > 18 mm	P value
(No, %)	(21 pt, 15.6%)	(84 pt, 62.2%)	(22 pt, 16.3%)	(8 pt, 5.9%)	
Age (yrs) (Mean ± std.dev)	37.9 ±12.6	47.6 ±17.04	46.6 ±17.25	48.38 ± 27.02	<0.05* Cc. 0.211
Biliary colic	5	29	3	4	>0.05
Obstructive Jaundice	13	47	19	4	>0.05
Biliary pancreatitis	3	8	0	0	<0.05*
T-bill (up to 1 mg/dl)	7.2 ± 7.99	5.70 ± 5.47	7.20 ± 7.4	7.7 ± 8.1	>0.05
D bill (up to 0.25mg/dl)	5.5 ± 6.03	4.1 ± 4.2	5.4 ± 6.3	5.7± 6.3	>0.05
AST(up to 37 IU/dl)	180.1 ± 152.1	149.4 ± 163.7	121.5 ± 116.2	107.1± 65.9	>0.05
ALT(up to 40 IU/dl)	279.7 ± 194.3	181.2 ± 166.5	154.7 ± 143.3	134.3 ± 146.5	<0.05* Cc (-0.191)
ALP (up to 100 IU/dl)	222.2 ± 110.5	293.1 ± 199.9	455.3 ± 202.9	290.9 ± 195.0	<0.05* Cc (0.368)

Cc: correlation coefficient. Pt: patients.

Table 4. Age, gender, nationality, presentation and LFTs in patients with and without CBD stones: ANOVA (logistic regression).

Parameter	CBD stone	No CBD stone	P value
Number	76 (56.3%)	59(43.7%)	> 0.05
Age	46.4 ±18.27	45.18 ±16.21	>0.05
Gender	F=45 (59.2%)	F=37 (62.7%)	>0.05
Nationality	S=54(71%)	S=35(59.3%)	>0.05
biliary colic	26(34.2%)	15(25.4%)	>0.05
Obstructive Jaundice.	47(61.8%)	36(61%)	>0.05
Biliary pancreatitis.	3(4%)	8(13.6%)	<0.05*
GB stones	43 (56.6%)	40 (67.8%)	>0.05
Cholecystectomy	13 (17.1%)	0(0%)	<0.001*
T. bilirubin	6.36± 7.16	6.2 ± 5.6	>0.05
D. bilirubin	4.7± 5.44	4.5 ± 4.6	>0.05
ALT(up to 40 IU/dl)	220.62 ± 194.8	171.1 ±143.3	<0.05*
AST(up to 37 IU/dl)	158 ± 153.6	134.6 ± 147.9	>0.05
ALP (up to 100 IU/dl)	321.8 ± 192.3	287.9 ± 207	<0.05*

and patient's age, presentation and liver function tests (LFTs). There is a significant positive correlation between CBD diameter and both age and serum ALP (correlation coefficient, 0.211and 0.368 respectively), also, there is a significant negative correlation between CBD diameter and ALT level (correlation coefficient, -0.191), it is also noted that all cases presented with biliary pancreatitis had CBD diameter less than 13 mm. Table 4 showed CBD stones predictors; ALT and ALP are significantly higher in patients with CBD stones while biliary pancreatitis are significantly more in patients without CBD stones. There were GB stones in 83 patients (61.5%) and post-cholecystectomy state in 13 patients (9.6%). All post cholecystectomy patients had CBD stones (highly significant difference). Table 5 showed the sensitivity and specificity of abdominal US in detecting CBD stones (69.5 and 88.1% respectively) and positive and negative predictive values (86.9 and 71.8%). ERCP is the gold standard in detecting CBD stones.

Abdominal ultrasound study was not conclusive for CBD stones in 21.3% of cases.

DISCUSSION

In this study, we tried to define the characteristics of ERCP patients as an indicator of biliary disorders in Makkah, Eastern province of Saudi Arabia. The female to male ratio was 1.56:1 and the mean age was 46.59 ± 17.6 yrs (range 17 to 85). In a study from Al-Khobar

Table 5. Abdominal ultrasound sensitivity and specificity in detection of CBD stone.

	ERCP (%)	US (%)	US sensitivity (%)	PPV (%)	US specificity (%)	NPV (%)
CBD stone(76)	56.3	39.1	69.5	86.9	88.1	71.8
no CBD stone(59)	43.7	49.6				

NPV: Negative predictive value; PPV: Positive predictive value.

(Eastern province, Saudi Arabia), the female to male ratio was 1:1 and the mean age was 45.2 ± 16.7yrs (range 10 to 98) (Al Qurane et al., 1996). In two studies from Egypt, the female to male ratio was 2.4:1 and 2:1, the mean age was 55 and 45 yrs(range: 17 to 64 and 27to 65) (El-Ghareeb et al., 2004; Ghazal et al., 2009), and in a study from Pakistan the female to male ratio was 4.3/1 (Durrani et al., 2007). From those data, the male percentage is higher and the mean age is lower in Saudi Arabia than those in Egypt and Pakistan, this may be related to the higher socioeconomic status and the effect of high fat diet.

Seven patients had DM, three of them had malignancy of the pancreas and biliary tree, the association between cancer pancreas and diabetes mellitus proved in a large cohort study in the USA (Coughlin et al., 2004).

Eleven patients had biliary pancreatitis (8.1%) and female to male ratio was (4.5/1). The number of patients is too small to be representative, in five studies from Riyadh the average female to male ratio was 2:1 (Al-Mofarreh et al., 1992; Matar, 2007; Singal et al., 2003; Al-Salamah and Bismar, 2002; Zahrani and Mansour, 2001). There was CBD stones in only 3 patients (27%); similar results came from Riyadh (26 and 16%) (Matar, 2007; Al-Salamah and Bismar, 2002) and from Jizan (18%) (Singal et al., 2003). The low percentage of CBD stones in biliary pancreatitis was observed before, where 85 to 90% of acute biliary pancreatitis patients improved clinically as the stone pass spontaneously (Virgilio et al., 1994; Acosta and Ledesma, 1974), also the percentage of CBD stones decreased dramatically by delaying ERCP (Al-Mofarreh et al., 1992). Urgent ERCP showed CBD stones in 75% of cases and delayed ERCP showed only 11% of CBD stone (Neoptolemus et al., 1986) and the same was noticed by Schwesinger et al. (1991) who reported that waiting 3 to 5 days, deceased the chance of finding associated CBD stones from approximately 70 to 20%. Most probably, biliary pancreatitis developed when a stone small enough to pass through the ampulla and obstruct the pancreatic duct while going out. In this study all of biliary pancreatitis patients had CBD diameter less than 13 mm, so, dilated CBD may be protective against biliary pancreatitis.

There is no significant difference in ERCP patients between Saudi and non Saudi. This signified the environmental factors especially the diet and lessen the racial factor. In this study, the female to male ratio in patients with GB stone was 1.7/1, in Jeddah the ratio was 4.6:1 (Zahrani and Mansour, 2001) and in USA the ratio was 4:1 (Schirmer et al., 2005). Reports from Africa and Asia showed the ratio of 2:1 (Ethiopia) (Getachew, 2008), 1.8:1 (India) (Verma et al., 2011) 1.8/1 and 2/1 (Iran) (Farzaneh et al., 2007; Massarrat, 2001), and a lower percentage in East Asia 1.4:1 (China) (Zhu et al., 1995), and from Korea the female predominance was not found (F/M=1.17/1.37) (Park et al., 2003). The increased prevalence of gallstone disease in women has been explained by its relation to oestrogen therapy and child birth (Jorgensen, 1988), while increasing male ratio may be related to high fat in diet.

There is a significant negative correlation between CBD diameter and biliary pancreatitis and a significant positive correlation between CBD diameter and both age and serum alkaline phosphate level. Usually biliary pancreatitis is less in old age and patients with dilated CBD. Also, there is a significant negative correlation between CBD diameter and ALT level which could be explained that markedly dilated CBD happened usually in chronic cases with less peri-billiary hepatitis.

In this study, 56.3% of patients had CBD stones and the predictors of presence of CBD stones are high ALT and high ALP, while biliary pancreatitis are significantly more in patients without CBD stones, most probably, stone passed after causing pancreatitis. These results are supported by results from Riyadh where the predictors for the presence of CBD stones were CBD diameter more than 7 mm, associated cholangitis, high bilirubin level at the day before ERCP, and high ALP level (Al Salamah and Bismar, 2002). In a study from Egypt, the incidence of CBD stones was 34% and the CBD stones predictors include; age >60 years, fever >37.6°C, raised levels of serum amylase, raised levels of ALP, dilated CBD >8 mm or stones on US–(El-Ghareeb et al., 2004). Bose and colleges found CBD stones in 29.5% and the risk factors were jaundice and high ALP (sensitivity 69%) while the presence of pancreatitis had low sensitivity (12%) (Bose et al., 2000). Elevation of serum bilirubin, AST and ALP and dilated common bile duct on US are also predictors for presence of CBD stones in other two studies (Onken et al., 1996; Leitman et al., 1993).

The sensitivity and specificity of abdominal US in

detecting CBD stones were 69.5 and 88.1% respectively,and positive and negative predictive values were 86.9 and 71.8%. In another study, US sensitivity and negative predictive value were 50 and 82% (Bose et al., 2000), as a general the sensitivity of ultrasound for detection of CBD stones ranged from 10 to 63% (Lichtenbaum et al., 2000).

Conclusion

In Makkah, patients referred for ERCP are similar to patients in other areas in Saudi Arabia and there is a non significant difference between Saudi and Non Saudi patients. Male are more prone to have biliary disorders than males in neighbour countries which may be related to the higher socioeconomic status and high fat diet. Malignancy should be suspected in old age diabetic patients presented with jaundice. Biliary pancreatitis is more in female patients and usually they have low incidence of CBD stones and CBD diameter of less than 13 mm. Predictors of CBD stones are previous cholecystectomy, high ALT and high ALP serum levels. It is advised to do ERCP before or during cholecystectomy in patients with positive predictors for CBD stones. Abdominal ultrasound is still considered as a good screening tool for the detection of CBD stones (specificity 88.1%).

ACKNOWLEDGEMENT

REFERENCES

Acosta JM, Ledesma CL (1974). Gallstone migration as a cause of acute pancreatitis. N. Engl. J. Med., 290: 484-487.

Al-Mofarreh MA, Laajam MA, Tikoo NM, Mohammed AM, Al-Shbaily FS, Alam MK (1992). The role of ERCP in the management of gallstone-associated acute pancreatitis: A prospective study of 64 patients at Riyadh Central Hospital. Ann. Saudi Med., 12(4): 334 - 338.

Al Qurane A, Ibrahim EM, Sultan AI (1996). Diagnostic and therapeutic value of ERCP and prediction of outcome: A retrospective analysis. Saudi J. Gastroenterol., 2(3): 138–141.

Al-Salamah SM, Bismar HA (2002). Role of preoperative endoscopic retrograde Cholangio-pancreaticography in the management of mild to moderate acute biliary pancreatitis. Saudi J. Gastroenterol., 8(3): 85-92.

Anderson SW, Rho E, Soto JA (2008). Detection of biliary duct narrowing and choledocholithiasis: accuracy of portal venous phase multi-detector CT. Radiology, 247(2): 418-427.

ASGE Guidelines (2010). The role of endoscopy in the evaluation of suspected Choledocholithiasis. Gastrointest. Endosc., 71(1): 1-9.

Barbara L, Sama C, Morselli LAM (1987). A population study on the prevalence of gallstone disease: the Sirmione study. Hepatology, 7: 913-917.

Bose SM, Mazumdar A, Kocher R, Katariya S, Pathak CM (2000). Evaluation of the Predictors of Choledocholithiasis: Comparative Analysis of Clinical, Biochemical, Radiological, Radionuclear, and Intraoperative Parameters. Surg. Today, 31(2): 117-122.

Caddy GR, Tham TC (2006). Gallstone disease: Symptoms, diagnosis and endoscopic management of common bile duct stones. Best Pract. Res. Clin. Gastroenterol., 20(6): 1085-101.

Coughlin SS, Calle EE, Teras LR, Petrelli J, Thun MJ (2004). Diabetes mellitus as a predictor of cancer mortality in a large cohort of US adults. Am J Epidemiol., 15; 159(12): 1160-1167.

Durrani AA, Yaqoob N, Husain Z, Siddique M, Moin S, Mufti MM (2007). Post-cholecystectomy complications and ERCP. Pak. J. Med. Sci., 23(4): 614-619.

Edmundowicz SA, Aliperti G, Middleton WD (1992). Preliminary experience using endoscopic ultrasonography in the diagnosis of choledocholithiasis. Endoscopy, 24(9): 774-8.

El-Ghareeb MH, Sami HA, El-Serafy MA (2004). The value of MRCP and ERCP in management of suspected common bile duct stones in patients with gallstone disease. Egypt. J. Surg., 23(1): 38-42.

Farzaneh E, Zavvareh HT, Gharadaghi J, Sheikhvatan M (2007). Prevalence and characteristics of gallstone disease in an Iranian population: a study on cadavers. Hepatobiliary Pancreat. Dis. Int., 6(5): 509-512.

Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ (1996). Complications of endoscopic biliary sphincterotomy. N. Engl. J. Med., 335: 909-918.

Getachew A (2008). Epidemiology of gallstone disease in Gonder University, Ethiopia Ethiopian. J. Health Dev., 22(2): 206-211.

Ghazal AH, Sorour MA, El-Riwini M, El Bahrawy H (2009). Single-step treatment of gall bladder and bile duct stones: a combined endoscopic-laparoscopic technique. Int. J. Surg., 7(4): 338- 46.

Johnson CD (2001). ABC of the upper gastrointestinal tract; Upper abdominal pain: Gall bladder. BMJ. 323: 1170-1173.

Jorgensen T (1988). Gall stones in a Danish population: fertility period, pregnancies, and exogenous female sex hormones. Gut, 29(4): 433-9.

Ko CW, Lee SP (2002). Epidemiology and natural history of common bile duct stones and prediction of disease.

Gastrointestinal endoscopy 56 (Suppl 6): S165–S169.

Kratzer W, Mason RA, Kachele V (1999). Prevalence of gallstones in sonographic surveys worldwide. J. Clin. Ultrasound, 27(1): 1-7.

Lai ECS, Mok FPT, Tan ESY (1992). Endoscopic biliary drainage for severe acute cholangitis. N. Engl. J. Med., 326: 1582-1586.

Leitman IM, Fisher ML, McKinley MJ (1993). The evaluation and management of known or suspected stones of the common bile duct in the era of minimal access surgery. Surg. Gynecol. Obstet., 176: 527-533.

Lichtenbaum, RA, McMullen HF, Newman RM (2000). Preoperative abdominal ultrasound may be misleading in risk stratification for presence of common bile duct abnormalities. Surg. Endosc., 14(3): 254-257.

Majeed AW (1999). Common duct diameter as an independent predictor of choledocholithiasis: is it useful? Clin Radiol., 54(3): 170-172.

Massarrat S (2001). Prevalence of gallstone disease in Iran. J. Gastroenterol. Hepatol., 16: 564-567.

Matar ZS (2007). The clinical pattern of acute pancreatitis: Al Kharj Experience. Internet J. Surg., 11(1): 27.

Metcalfe MS (2004). Is laparoscopic intraoperative cholangiogram a matter of routine? Am J Surg. 187(4): 475-481.

Neoptolemus JP, London NJ, Slater ND (1986). A prospective study of ERCP and endoscopic sphincterotomy in the diagnosis and treatment of gallstone acute pancreatitis. Arch. Surg., 121: 697-702.

Onken JE, Brazer SR, Eisen GM, Williams DM, Bouras EP, DeLong ER (1996). Predicting the presence of choledocholithiasis in patients with symptomatic cholelithiasis. Am. J. Gastroenterol., 91: 762-767.

Park SJ, Kim SW, Park YC, Kim YT, Yun YB, Park YH (2003). Clinical and epidemiological analysis of a 20-year experience of surgically treated gallstone patients. Korean J. Gastroenterol., 42: 415-422.

Rosseland AR, Glomsaker TB (2000). Asymptomatic common bile duct stones. Eur. J. Gastroenterol. Hepatol., 12(11): 1171-1173.

Sauerbruch T, Baumgartner G (1991). Gallbladder stones: management. Lancet, 338: 121-124.

Scaffidi MG (2009). Magnetic resonance cholangio-pancreatography versus endoscopic retrograde cholangio-pancreatography in the diagnosis of common bile duct stones: a prospective comparative study. Minerva Med., 100(5): 341-348.

Schirmer BD, Winters KL, Edlich RF (2005). Cholelithiasis and cholecystitis. J. Long Term Eff. Med. Implants, 15(3): 329-338.

Schwesinger WH, Page CP, Siriknek KR (1991). Biliary pancreatitis: Operative outcome with a selective approach. Arch. Surg., 126: 836-840.

Singal AK, El Amin AK, Ayoola AE (2003). Profile of acute pancreatitis in Jizan, Saudi Arabia, Saudi Med. J. 1: 72-75.

Tazuma S (2006). Gallstone disease: Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best Pract. Res. Clin. Gastroenterol., 20: 1075-1083.

Topal B, Van de Moortel M, Fieuws S (2003). The value of magnetic resonance Cholangio-pancreatography in predicting common bile duct stones in patients with gallstone disease. Br. J. Surg., 90: 42-47.

Tse F (2008). EUS: a meta-analysis of test performance in suspected choledocholithiasis. Gastrointest. Endosc., 67(2): 235-244.

Verma A, Mohan S, Baijal SS (2011). Ultrasonographic evaluation of asymptomatic gall bladder stones in north India. J. Clin. Diag. Res., 5(2): 328-330.

Virgilio C, Verbin C, Chang L, Linder S, Stabile BE, Klein S (1994). Gallstone Pancreatitis: The Role of Preoperative Endoscopic Retrograde Cholangio-pancreatography. Arch. Surg., 129: 909-913.

Williams EJ (2008). Guidelines on the management of common bile duct stones (CBDS). Gut. 57(7): 1004-1021.

Yusoff IF, Barkun JS, Barkun AN (2003). Diagnosis and management of cholecystitis and cholangitis. Gastroenterol. Clin. North. Am., 32: 1145-1168.

Zahrani IH, Mansour I (2001). Gallbladder pathologies and cholelithiasis. Saudi Med. J., 22(10): 885-889.

Zhu X, Zhang S, Huang Z (1995). The trend of the gallstone disease in China over the past decade. Zhonghua Wai Ke Za Zhi, 33: 652-658.