

## Changing Pattern and Incidence of Gallstone Diseases in Al-Kadhymia Teaching Hospital

Bashar A Abdul Hassan *CABMS; FIBMS*

Dept. of Surgery, College of Medicine, Al-Nahrain University

### Abstract

**Background** Gallstone diseases remain a common health problem for human, affecting millions of people throughout the world. In Iraq, recent years has shown an increasing number of patients with gallstones with concurrent decreasing age of presentation, risk factors have been assessed taking in consideration the effect of stressful life events that Iraqi peoples had been suffered during these years on the development of gallstone diseases.

**Objective** To give an idea about, and possible causes for the changing in number, age of presentation and trend of surgical management of gallstone diseases in Iraq.

**Methods** Clinical assessment and risk factors assay including stressful life events were done for 1226 patients who have been cholecystectomised over seven years from Jun 2002 to Jun 2009 in Al-kadhymia Teaching Hospital.

**Results** Significant increases in the number of symptomatic gallstone cases were noted, nearly 50% of them presented with abdominal pain, more than half of patients were young in the 3<sup>rd</sup> and 4<sup>th</sup> decades, female to male ratio was 5.9:1 and decreasing with age, 74% of patients had BMI > 25% (over weight), impact of stressful life event was obvious in the recent years on nearly two third of patients with gallstone diseases, minimal invasive technique (laparoscopic surgery) was evolving and most of the cases now done by this method.

**Conclusions** Gallstones diseases are increasing in our country with obvious decrease in the age of presentation, this might be due to stressful life events to which Iraqi peoples had been exposed, and also the revolution of minimal invasive surgery had a great impact in the management of this disease.

**Key words** Pattern, Incidence, Gallstone diseases.

### Introduction

Gall stones are the most common biliary pathology, 10 to 15% of adult population in the USA had gallstones <sup>(1)</sup>, while as high as 60% of pima Indians over 35 years of age <sup>(2)</sup> and as low as in Japanese women 3.2 % <sup>(3)</sup>, no accurate record of the incidence or prevalence of gall stones in Arab countries <sup>(4)</sup>, for a long time this disease was known to be of fatty fertile fifty female <sup>(5)</sup>, these facts need to be reviewed, there has been a significant increase in the incidence

of gallstones in patient under 30s of age in the past 10 years <sup>(6)</sup> also there is a change toward asthenic female <sup>(7)</sup>.

There was a change in the management approach toward minimal invasive surgery as first option <sup>(8)</sup>. In this study we tried to evaluate the effect of risk factors on these changes, especially the effect of stressful life events in Iraq in the recent previous war years in which Iraqi peoples had been exposed to different harmful

psychological events that have their obvious effect on many serious illnesses including gallstones, thyroid, and various malignant diseases in Iraq<sup>(9)</sup>.

### Methods

A prospective study conducted in Al Kadhymia Teaching Hospital in the period from June 2002 to June 2009, during these years 1226 patients to whom cholecystectomy had been done (open or laparoscopic surgery) for gall stone diseases, other indications have been excluded from the study like trauma and a calculus cholecystitis.

After detailed history and thorough clinical examination, the diagnosis was confirmed by ultrasound examination, special attention was given to risk factors; age, sex, fertility, weight (represented as body mass index, BMI), family history and history of exposure to stressful life events like loss of close relatives, loss of job, loss of house due to sectarian migration and poverty, especially that what happened during and after year 2003 (**guerrilla warfare**). Analysis of these risk factors and their significant effects had been done.

### Results

A total number of 1226 patients who had gall stones, over these years a significant increase in the number of admission for patients with gallstone diseases in relation to total admission to the surgical ward e.g. in 2002 it was 7% increased steadily to 16% of the total admission in 2009, the highest incidence noticed in years 2008-2009 about 25% of all cases included in the study, the least number of elective operation is that of year 2003-2004 about 6.5% of all cases as shown in table 1 and figure 1.

Clinically the majority of the patients (43.8%) presented with abdominal pain either epigastric

or right hypochondrial, other presentation like non specific dyspeptic symptom, indigestion, heart burn or complication in which acute cholecystitis is the commonest (19.4%), incidental finding was in (4.8%) and carcinoma of the gall bladder was the least complication (1.01%) as shown in table 2.

### Regarding risk factors

**Age** range was 17-75 years with a mean age of 45.3 years; the majorities were in the 3<sup>rd</sup> and 4<sup>th</sup> decades as shown in table 3.

**Sex**; the majority of patients were females 1049 compared to 177 males with over all females to males ratio (5.9:1), this ratio decreased with age (2.2:1 for those aged > 50) as number of male patients increases with age, see figure 2.

**Fertility**: Reproductive data shows that 963 females were fertile ( $p < 0.001$ ) were as only 86 were unmarried or infertile.

**Obesity**; the relation of obesity, BMI with gallstone formation is compared in table 4, 74% of the overall patients were overweight (BMI > 25), 47% were obese (BMI > 30%), 4.4% were morbidly obese (BMI > 40%) as shown in table (4).

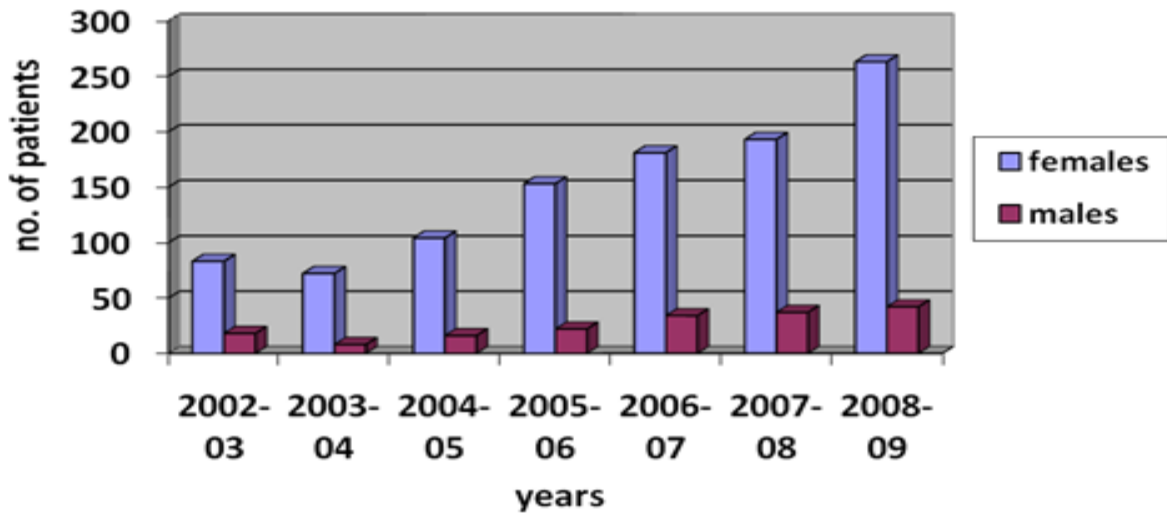
**Family history** of gall stones diseases (first degree relatives) found in 32% of female patients ( $p < 0.01$ ), while male patients only 5.3%.

**Life stress**; Definite history of stressful life events was linked to 21% of those patients in the years 2002 to 2004 while 63% of those in years following the war ( $p < 0.001$ ).

**Surgical approaches**; Minimal invasive surgery played a major role in the management of patient in the last years of the study, while majority of cases in the early years of the study were operated upon by the usual open cholecystectomy as shown in table 5.

**Table 1. Distribution of patients by sex and age over the years of study**

June to June	No. & % both sex	No. & % females	No. & % males	No. patient aged < 40 yr	No. patient aged > 40 yr
2002-03	101 (8.2%)	83 (6.7%)	18(1.5%)	40	61
2003-04	80 (6.5%)	72 (5.8%)	8(0.6%)	21	59
2004-05	120 (9.7%)	104 (8.4%)	16(1.3%)	63	57
2005-06	175 (14.3%)	153 (12.5%)	22(1.8%)	94	81
2006-07	215 (17.5%)	181 (14.7%)	34(2.8%)	120	95
2007-08	230 (18.8%)	193 (15.7%)	37(3.0%)	145	85
2008-09	305 (25%)	263 (21.4%)	42(3.4%)	242	63
Total	1226 (100%)	1049 (85.6%)	177 (14.4%)	725 (59.2%)	501 (40.8%)



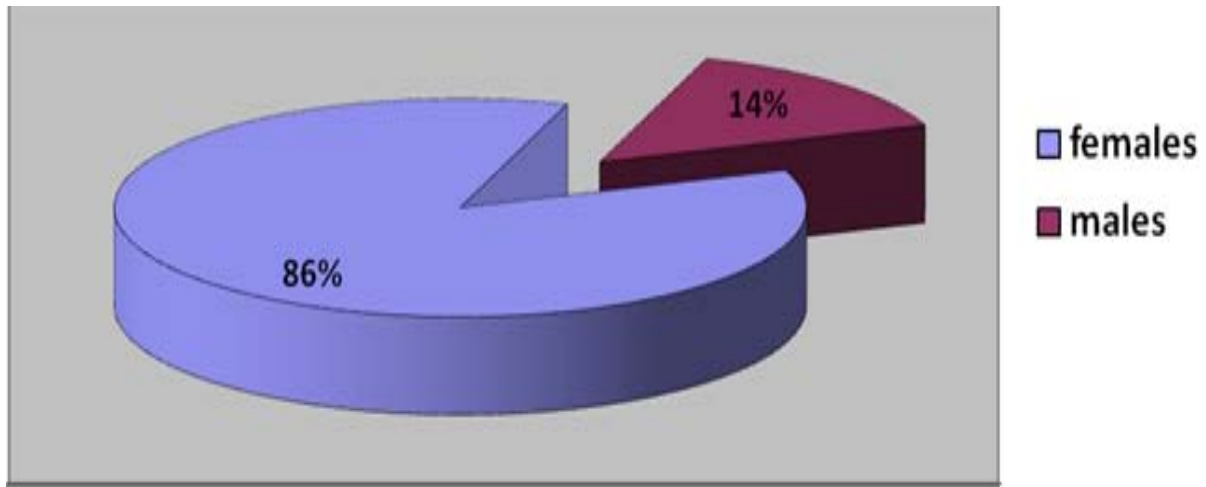
**Figure 1. Distribution of male and female patients.**

**Table 2. Clinical presentations of patients**

Symptoms	No.	%
Abdominal pain	537	43.8
Non specific dyspepsia	243	19.8
Complications;		
Cholecystitis	238	19.4
Obstructive jaundice	88	7.2
Empyaemia	28	2.3
Pancreatitis	18	1.45
Carcinoma	13	1.06
Incidental finding	61	4.97
Total	1226	100

**Table 3. Distribution by age of presentation**

Age / years	Number	%
< 20	43	3.5
20 -29	314	25.1
30-39	368	30
> 40	501	40.8
Total	1226	100



**Figure 2. Percentage of male and female patients**

**Table 4. Distribution of patients by (BMI)**

BMI kg/m <sup>2</sup>	No. of patients	percentage	<i>p</i> value
> 25	907	74%	< 0.001
> 30	576	47%	
> 40	54	4.4%	

**Table 5. Distribution of patients by the surgical approaches**

Years	Open surgery	%	Laparoscopic	%
1 <sup>st</sup>	78	12.2	23	3.8
2 <sup>nd</sup>	69	10.8	11	1.8
3 <sup>rd</sup>	87	13.6	33	5.5
4 <sup>th</sup>	128	20.1	47	7.9
5 <sup>th</sup>	98	15.4	117	19.8
6 <sup>th</sup>	74	11.6	156	26.4
7 <sup>th</sup>	102	16	203	34.4
Total	636	100	590	100

## Discussion

Gallstone disease is one of the most common and costly of all digestive diseases. Survey estimated that 6.3 million men and 14.2 million women aged 20 to 74 in the United States had gallbladder disease<sup>(10)</sup>.

Indeed, cholecystectomy is the commonest surgical procedure in the abdomen in the Western world<sup>(1)</sup>, in relation to the total yearly surgical discharge although the gallbladder operations increases, still cholecystectomies comes next to the frequency of appendicectomies; 1226 versus 1575 subsequently (over 7 years of study), conversely the incidence of gallbladder operations has been increasing and exceeded that for appendicectomies in observation in Jewish General Hospital, Montreal<sup>(11)</sup>.

In the current study, the hospital admission rates for cholecystectomy increased steadily among both sexes which reflect an increase incidence of gallstone in our population (the number of cholecystectomised patients has 98% correlation with the true incidence of gallstone<sup>(12)</sup>), this concurs with the finding in Queen Elizabeth hospital, Hong Kong, which shows an increase incidence of cholecystectomies from year 1981 to 1983<sup>(6)</sup>, this may be in part due the rise in calorie and fat consumption, decrease in fiber intake, and increased prevalence of the sedentary lifestyle in Iraq especially after year 2003 in Iraq, in Asian population the increase incidence of gallstone disease and hospital admissions for elective cholecystectomy was steady in the past decade due to the similar risk factors<sup>(13)</sup>.

In regard to the spectrum of symptoms of gall bladder diseases, a prospective study conducted at surgical department of Liaquat University of Medical and Health Sciences in Pakistan during 2001 to 2005 showed that 56% of patients presented with abdominal pain, others including acute cholecystitis in 36%, acute pancreatitis in

4%, obstructive jaundice and or cholangitis in 0.5% and gall bladder cancer in 0.3%<sup>(8)</sup>. In this series 43.8% of patients presented with abdominal pain, 19.8% with non specific dyspeptic symptom, 19.4% with acute cholecystitis, 7.2% with obstructive jaundice, 1.06 with abdominal mass (proved by histopathology as gall bladder carcinoma) and 4.97% incidentally found.

As most epidemiological studies in western literature, our findings reveal that females have higher frequency of gallbladder disease as males, over all (5.9:1), in western 4:1<sup>(14,15)</sup>. In older age group the female to male ratio decreases to 2.2:1 in our study, in western 2:1<sup>(14,16,17)</sup>, while this females predominance was not found in Korea<sup>(18)</sup>.

Stones are generally reported to be uncommon before the age of 20 years<sup>(19)</sup>, and 40 years is considered as a typical age at clinical diagnosis<sup>(20)</sup>. This relation to age is supported by the studies that showed that the sensitivity of the gallbladder to cholecystokinin (CCK) decreases with aging<sup>(21)</sup>, in our series 59.2% of patients were younger than 40, 25.1% bellow 30 years old and 3.5% bellow 20 years, these are comparable with that of the study done in Saudi Arabia by Murshid being that gallstones appear to be much more common in Saudi females and appear to occur at a considerably younger age 58% bellow 40 years, 31% bellow 30 years<sup>(4)</sup>, while our previous series in late eighties and nineties of the previous century in Iraq showed that the peak age incidence was between 40-50 years<sup>(22,23)</sup>.

Increased fertility is another important risk factor we found that 92% of female patients were fertile women. This factor appears to exert its influence through the hormonal changes occurring during pregnancy and is translated into a female: male ratio of gallstones which is much higher during the reproductive period than after

the menopause<sup>(24)</sup>. Ultrasound surveys of pregnant women have found an increase in gallbladder volume and reduced rates of emptying after liquid meals<sup>(25)</sup>. Others have reported a high prevalence of gallbladder sludge in women who were immediate postpartum although the sludge resolved within a year in most<sup>(26)</sup>. Jorgensen found a strong trend toward increasing stone prevalence with increasing childbirths, especially among women aged 30 years<sup>(27)</sup>. These above observations applied strongly to our patient's population with their relatively early menarche, early marriage and high parity<sup>(22)</sup>.

Majority of patients included in the study have BMI higher than 25 kg/m<sup>2</sup>. A well-established pathophysiologic link between obesity and gallstone formation is cholesterol-supersaturated bile<sup>(28)</sup>. Obese people hypersecrete biliary cholesterol, bile salts, and phospholipids, but the rate of cholesterol secretion supersedes that of the other biliary lipids, leading to cholesterol-supersaturated bile<sup>(29)</sup>. In theory, increased flux of cholesterol from the bile into gallbladder muscle cells stiffens the sarcolemmal membranes, decouples signal transduction, and inhibits gallbladder muscle function<sup>(30)</sup>. However, ultrasound data on gallbladder volume and emptying in obese humans are conflicting, while most studies suggest increased resting gallbladder volume in obese subjects; some reports demonstrate that these large gallbladders empty normally<sup>(31)</sup>.

The prevalence of symptomatic gallstone disease in the family study was significantly greater ( $p < 0.01$ ) in females as compared to males, 28% versus 6.6% respectively, which is comparable with our findings; 32% and 5.3% respectively. These data suggest that genetic factors are responsible for at least 30% of symptomatic gallstone disease. However, the true role of heredity in gallstone pathogenesis is probably higher because data based on symptomatic

gallbladder disease underestimates the true prevalence in the population<sup>(32)</sup>.

The changes that had been noticed in the incidence and age presentation of gallstones diseases in Iraqi peoples could not be attributed to the usual risk factors in stone formation, we believe that stressful life events (SLEs) might be more significant trigger for stones development. This study was carried over a very stressful period in the history of Iraq, characterized by war and economic sanction. These events put a severe burden on Iraqi people, so we propose, as suggested by previous workers in the field from different countries also subjected to the stress of similar events as in Serbia, Nigeria, or Portugal that stressful life conditions might be the cause of increase incidence of gall stone diseases<sup>(9)</sup>. In Atlanta – a new study led by Center for Behavioral Neuroscience researchers has determined that social stress leads to gall bladder dysfunction in the form of decreases motility and increases bile retention, a precursor to gallstone development in cichlid fish. The work could hold clues to whether similar stress in humans -- anxiety disorders, or work, status and money worries and the like -- can increase the risk of developing gallstones in Georgia patients<sup>(33)</sup>.

A study done by Geetha et al in China suggested that psychological stress is associated with increased oxidant production and oxidative damage, they noticed that gall stone patients have a high level of oxidative stress in the gall bladder mucosa, a finding that may be related to a decreased activity of functional enzymes in mucosal cells. Such a condition might result in an altered gall bladder absorption and secretion of bile components such as mucins and glycoproteins. The resultant increased risk of bile saturation would further contribute to the progress of gall stone formation<sup>(34)</sup>.

In Pakistan which had passed through war conditions and stress, Naseem, et al reported

that psychological stress is a risk factor for cholesterol gallstones formation<sup>(35)</sup>.

After the introduction of Laparoscopic cholecystectomy (LC) in 1991, its widespread use has completely revolutionized the management of cholelithiasis either simple or complicated and advantages of LC are undoubtable in comparison to open cholecystectomy and it has got economic advantages over open surgery<sup>(36)</sup>, it is obvious from our data results that minimal invasive technique (LC) for removal of gall bladder gradually becomes the standard method over the usual classical open cholecystectomy as shown above in table 5.

### Conclusions

The definite rise in the incidence and the decreased age of presentation of gallstones diseases could be due to increasing stressful life conditions affecting Iraqi population, but this should be studied more thoroughly well including all major governmental and private hospitals to be more precise and representative. In the years following 2003 in Iraq, a more westernized diet had been consumed, this may have an additive effect on the changes of gallstones diseases pattern and it is worthy to study this subject by special dietitian. The changing behavior toward more minimal invasive technique (laparoscopic surgery) is safe and better especially for the patients.

### References

1. Kevin C. The gall bladder and bile ducts. In: Williams NS, Bulstrode CJK and O'Connell PR. Baily and Love's short practice of surgery 25th ed. Arnold International students edition. London, 2008: 1119-1122.
2. Sampliner RE, Bennett PH, Comess LJ, Rose FA, and Burch TA. Gallbladder disease in Pima Indians N. *Engl J Med*, 1970; 283:1358-64.
3. Nomura H. Prevalence of gallstone disease in a general population of Okinawa, Japan. *Am J Epidemiol*, 1988; 128: 598-605.

4. Murshid KR. Symptomatic gallstones: A disease of young Saudi women. *Saudi J Gastroenterol*, 1998; 4: 159-162.
5. Russell RCG. The gall bladder and bile ducts. In: Charles VM and Russell RCG. Baily and Love's short practice of surgery 20<sup>th</sup> ed. EL: BS. London, 1990; p. 1060.
6. Ho HL, Liu HN, and Leung ML. Cholelithiasis in Young Chinese under 30 years of age-incidence and presentation. *Hong Kong Medical association*, 1985; 37(3): 144-145.
7. Gupta RL, Sharma SB, Kumar SP, and Monika. Changing trends (Clinico-biochemical) in gall-bladder stone disease- an observation. *Indian J Med Sci*, 1998 Jul; 52(7): 309-316.
8. Addul Aziz LK, Talpur AH, and Malik AM. Laparoscopic Cholecystectomy in complicated gallstone disease. *J Liaquat Uni Med Health Sci*, 2008; 7(1): 18-24.
9. Sulaiman TI. Changing patterns of thyroid pathology and trend of surgical treatment. *J Arab Board Health Specializations*, 2009; 10(2): 13-9.
10. Everhart JE, Khare M, Hill M, and Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. *Gastroenterology*, 1999; 117: 632.
11. Margolese R, Mitmaker B, Teitlebaum D and Ballo H C. Observation on the Incidence of Gallstone Disease. *Canada Med Ass J*, 1963 88(18): 1033-1035.
12. Andersson A, Bergdahl L, and Boquist L. Acalculous cholecystitis. *American J Surg*, 1971Jul; 122(1): 3-7.
13. Huang J, Chang C H, Wang J L, Kuo HK, Lin JW, Shau WY and Lee PH. Nationwide epidemiological study of severe gallstone disease in Taiwan. *BMC Gastroenterology*, 2009; 9: 63.
14. Everhart JE, Khare M, and Hill M. Prevalence and ethnic differences in gallbladder disease in the United States. *Gastorenterology*, 1999; 117: 632-639.
15. Friedman GD, Kamel WB, and Dawber TR. The epidemiology of gallbladder disease: Observations in the Framingham Study. *J Chron Dis*, 1966; 19: 273-292.
16. GREPCO (Rome Group for the Epidemiology and Prevention of Cholelithiasis). Prevalence of gallstone disease in an Italian adult female population. *Am J Epidemiol*, 1984; 119: 796-805.
17. Barbara L, Sama C, and Morselli Labate AM. A population study on the prevalence of gallstone disease: The Sirmione study. *Hepatology*, 1987; 7: 913-917.
18. Park YH, Park SJ, and Jang JY. Changing pattern of gallstone disease in Korea: *World J Surgery*, 2004; 28: 206-210.

19. Andrassy RJ, Treadwell TA, Ratner IA, and Buckley CJ. Gallbladder disease in children and adolescents. *Am J Surg*, 1976; 132: 19-21.
20. Diehl AK, Stem MP, Ostrower VS, and Friedman PC. Prevalence of clinical gallbladder disease in Mexican-American, Anglo and Black women. *South Med J*, 1980; 73: 438-441.
21. Khalil T. Effect of aging on gallbladder contraction and release of cholecystokinin-33 in humans. *Surgery*, 1985; 98: 423-429.
22. Al-AJDA KI. Gall bladder diseases. A thesis submitted to department of general surgery Baghdad University, 1988; p. 45-46.
23. AL-KASS SY. Composition of gallbladder stones and bile in cholelithic patient. A thesis submitted to the faculty of Medicine University of Basrah, 1892; p. 78-79.
24. Diehl AK. Epidemiology and Natural History of gallstone disease. *Gastroenterol Clin NA*, 1991; 20: 1-19.
25. Braverman DZ, Johnson ML, and Kern JF. Effects of pregnancy and contraceptive steroids on gallbladder function. *N Engl J Med*, 1980; 302: 362-364.
26. Maringhini A. Sludge and stones in gallbladder after pregnancy. Prevalence and risk factors. *J Hepatol*, 1987; 5: 218-223.
27. Jorgensen T. Gallstones in a Danish population. Fertility period, pregnancies and exogenous female sex hormones. *Gut*, 1988; 29:433-9.
28. Amaral JF, and Thompson WR. Gallbladder disease in the morbidly obese. *Am J Surg*, 1985; 149: 551-557.
29. Carey MC, and Small DM. The physical chemistry of cholesterol solubility in bile. Relationship to gallstone formation and dissolution in man. *J Clin Invest*, 1978; 61: 998-1026.
30. Yu P, Chen Q, and Harnett KM. Direct G protein activation reverses impaired CCK signaling in human gallbladders with cholesterol stones. *Am J Physiol*, 1995; 269: G659-G665.
31. Vezina WC, and Paradis RL. Increased volume and decreased emptying of the gallbladder in large (morbidly obese, tall normal, and muscular normal) people. *Gastroenterology*, 1990; 98: 1000-1007.
32. Nakeeb A, Comuzzie AG, Martin L, Sonnenberg GE, Swartz-Basile D, Kissebah AH, and Pitt HA. Gallstones Genetics versus Environment. *Ann Surg*, 2002; 235(6): 842-849.
33. Earley RL, Blumer LS, and Grober MS. The gall of subordination: changes in gall bladder function associated with social stress. *Proc R Soc Lond B*, 2004; 271, 7-13.
34. Geetha A. Evidence for oxidative stress in the gall bladder mucosa of gall stone patients. *J Biochem Mol Biol Biophys*, 2002; 6: 427-443.
35. Channa NA, Khand FD, Khand TU, Leghari MH, and Memon AN. Analysis of human gallstones by Fourier Transformation Infrared (FTIR). *Pak J Med Sci*, 2007; 23(4): 546-550.
36. Kuzin NW, Dadvani SS, Vetshev PS, Kharnas SS, Safronov VV, Kashevarov SB. Laparoscopic and standard cholecystectomy: comparison of immediate results. *Khirurgii (Mosk)*, 2000; 2: 25-7.

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Correspondence to: Dr. Bashar A Abdul Hassan,

E-mail: basharabass@yahoo.com

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