Sociological Risk Factors in the Development of Gallstones for Women in the Childbearing Age a Case-control study

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Abstract:

Background: Gallstones are highly prevalent in most countries all over the world. Although most of gallstones are asymptomatic, complicated stones lead to important morbidity and complications, and to high costs of medical care, making gallstone prevention highly desirable. The exact etiology of gallstones formation is still unknown, but there are many risk factors that have been proved scientifically to be important contributors for gallstones occurrence. Most of these risk factors are highly related to the ways of human living in modern ages such as unhealthy dietary behaviors and sedentary life. This suggests that sociological backgrounds play a crucial role in the initiation of this disease and the keys for the prevention of gallstones may be through the context of human life.

Aim & Objective: To examine sociological risk factors in the development of asymptomatic gallstones of women at childbearing ages attending X-ray department for doing abdominal ultrasound examination for other reason.

Study design: Case-control study, where 110 women with asymptomatic gallstones for the first time diagnosed by ultrasound examination without previous episodes of acidity and right hypochondrial pain were allocated as cases. Another 110 women proved to be without gallstones by ultrasound examination and without previous history of acidity or right hypochondrial pain episodes. Matching is done for age ± 5 years. Unpaired sampling technique had been used.

Study period: from 1st. October 2006 to 1st. February 2007.

Questionnaire: The questionnaire included assessment of sociological factors such as personal characteristics (social identity, personal habits and psychological make-up), life events (stress, social discontinuities and geographical mobility) and social context (economic factors, social integration, urbanization). In addition, body mass index, waist to hip ratio was also estimated and the state of parity for each woman participated in this research.

Results: Regarding *Personal Characteristics*; positive family history was found in this study to be highly associated with the development of gallstones (OR= 2.63, P-value= 0.004, 95%C.I.= 1.73-5.06), as well as sedentary life (OR= 3.97, P-value=0.0001and 95%C.I.= 1.99-7.91), unhealthy dietary behaviors (OR= 3.27, 0.0001, 95%C.I.= 1.89-5.67) and active smoking (OR= 3.32, P-value=0.019 and 95%C.I.= 1.22-9.05). According to *Life Events*; exposure to stress was found to be associated with the occurrence of gallstones (OR=3.00, p-value= 0.0001, 95%C.I. = 1.70-5.29), and social discontinuities (OR=2.62, p-value= 0.002, 95%C.I. = 1.43-4.79). Central obesity was also found to be associated with the development of gallstones (OR=2.18, P-value=0.004, 95% C.I. =1.27-3.73) as well as high parity (OR=3.47, P-value=0.0001, 95% C.I. = 2.01-6.00).

Conclusion: Positive family history, sedentary life, unhealthy dietary behavior, active smoking, stress, social discontinuities, abdominal obesity, and high parity all are among the important sociological risk factors in the development of gallstones for women in childbearing ages.

Key words: Sociological risk factors, gallstones, women, childbearing ages.

Introduction:

Gallstones are a major public health problem in both developed and developing countries. They represent a serious burden for the modern healthcare systems e.g., 10–20 % of Europeans and Americans carry gallbladder stones [1]. The prevalence of gallstone disease is rising, possibly as a result of longer life expectancy, altered nutritional habits and improved diagnostic technologies. Many gallstones are silent, but symptoms and complications arise in around 25–50% of cases, necessitating surgical removal of the gallbladder, usually by laparoscopic cholecystectomy [2,3].

Cholelithiasis incurs annual medical expenses in excess of $6 billion in the US and is currently the second most expensive digestive disease, exceeded only by reflux disease [4].

The clinical management of gallstone disease is almost exclusively based on cholecystectomy and endoscopic or medical treatment of complications. Gallstone disease is a disorder with an increasing prevalence, reflecting the increasing life expectancy and changes in life style in "westernized" societies. Thus, one can regard this disease as one of the chronic non-communicable diseases (diseases of human modern ages) that are mostly having multiple etiology and risk factors that are mainly originated from the way of living [6].

An improved etiological and pathophysiological understanding of gallstone disease may lead to novel, non-surgical, options for prevention and therapy. Significant progress has been made both in the genetics of gallstone

formation and in the molecular biology of bile excretion. Currently, most studies have used real time ultrasonography as a screening method in randomly selected populations. Ultrasonography does not only allow the assessment of prevalence, but it is also suitable for follow up in order to establish gallstone incidence and to define risk factors for gallstone disease [7].

Cholesterol gallstones constitute more than 80% of stones in the Western world[8]. Four main types of abnormalities have been considered to be responsible for cholesterol gallstone formation: (1) Bile super-saturation in cholesterol, (2) Enhanced nucleation of cholesterol crystals. (3) There also must be sufficient time for nucleation to occur. (4) Intestinal hypomotility has been recently recognized as a fourth primary factor in cholesterol lithogenesis.

Gallstone formation is multi-factorial and includes two main domains: The first one is constitutional (un-modifiable) such as female gender, increasing age, ethnicity, and positive family history. The second one is environmental (modifiable) risk factors competing to litho-genesis such as obesity, rapid weight loss, hyper-triglyceridaemia, drugs lowering serum cholesterol, slow intestinal transit, gallbladder stasis, unhealthy dietary behaviors (such as high caloric diet, highly absorbable sugars, low fiber diet, low calcium and low vitamin C diet) in addition to the smoking and sedentary behaviors[9,10].

It is clearly seen that most of the upper risk factors are highly related to the mode of living of the human, and to a large extent, they are culturally and socially determined behaviors that could be changed in favor for the prevention of this disease, rather than in way of prompt treatment, since they are mostly controllable ones.

Subject & Methods:

In order to achieve the aim of the present study, a case-control study design was adopted, 110 with asymptomatic newly diagnosed gallstones were enrolled in this study as cases according to the following inclusion criteria:

-The participant must be a woman, in the childbearing age.
-For the first time, is proved to have gallstones by ultrasound examination.
-Negative previous history of having acidity or right hypochondrial pain episodes.

Another 110 women were chosen as control for this study with the following inclusion criteria:

-The participant must be woman, in childbearing age.
-Negative history to any previous episode for acidity or right hypochondrial pain episodes.
-Proved by ultrasound examination for the first time not to have gallstones.

Both cases and controls were achieved at the X-ray Institute that belongs to the Mosul College of Medicine. Asymptomatic only subjects were enrolled in the study in order to eliminate the effect of recalling bias in this type of study.

Un-paired sampling technique was used in this study, matching was done for age (± 5 years). Every woman in this study was interviewed by the researchers and the following questions to participants were answered in addition to the specific anthropometric measurements such as, BMI, WHR.

Social factors in health and Disease [11]:

I – Personal characteristics:

A- Social identity:

Not modifiable: age, sex and heredity (family history of gallstones in primary relatives)
Modifiable as marital status, occupation, and race.

B- Personal habits: Lifestyle
Sedentary life style.
Smoking.
Alcohol consumption.

Fatty, calorie and salt rich diets (unhealthy diets)

C- Psychological make-up:
Personality type A
Personality type B

II – Life Events:

A- Stress

B- Social discontinuities:
Death of spouse
Change in marital status (divorce, recent marriage, single or widowed)
Retirement and change in the job
Change of residence
The birth of new baby

C- Geographical mobility:
- Rural to urban (urbanization)

D- Catastrophic events: such as terrorist events.

III – Social Context:

A- Economic factors:
- Unemployment.
- Very high employment
- Sudden job descend.

- Sudden loss of huge money.

B- Social integration
- Living alone, or with family

C- Urbanization:
- Urban or rural
- Crowding index

D- Social Class

The Odd ratio was then calculated for every risk factors of the concern in this study with its p-value. Special statistical analysis was used (SPSS and Minitab) to examine the effect for results in this study.

Results:

The mean age of the study population was 41.3 years for cases and 42.1 years for controls. The results of examining social risk factors in the development of gallstones appeared as the following:

Table (1) shows the distribution of cases and controls according to personal characteristics and reveals in regarding to social identity that positive family history (which is one of unmodifiable risk factor) was found to be associated with the development of gallstones (OR= 2.63, P-value= 0.004, 95%C.I. = 1.73-5.06), while the presence of abnormal marital status (as single, divorced and widowed) was not related for the development of gallstones. This table (regarding personal habits) also indicated that sedentary life was risky for persons in the development of gallstones (OR= 3.97, P-value=0.0001 and 95%C.I.= 1.99-7.91), the habit of cigarette smoking was moreover associated with occurrence of gallstones (OR= 3.32, P-value=0.019 and 95%C.I.= 1.22-9.05), Regarding unhealthy dietary habits (rich fatty, calorie and salt intake), this risky behavior appeared to be highly associated (OR= 3.27, 0.0001, 95%C.I.= 1.89-5.67) with the development of gallstones, but alcohol consumption appeared in this study to do nothing in the causation of this disease. Finally regarding psychological make up, personality type A, appeared to be not associated with the occurrence of gallstones.

Table (1): Distribution of the study population according to personal characteristics

Factor	cases		controls		O R	P-value	95 % C.I.
	No.	%	No.	%			
+ve family history	34	30.91	16	14.55	2.63	0.004	1.73-5.06
Chang in marital state	3	2.73	9	8.18	0.32	0.075	0.09-1.12
Sedentary life	36	32.73	12	10.91	3.97	0.0001	1.99-7.91
Active smoking	15	13.64	5	4.55	3.32	0.019	1.22-9.05
Alcohol consumption	0	0.00	0	0.00	1		
High fatty, calorie and salt intake	78	70.91	47	42.73	3.27	0.0001	1.89-5.67
Personality type A	63	57.27	48	43.64	1.73	0.043	1.02-2.94

Table (2) indicates that stressful life events were highly associated with the development of gallstones (OR=3.00, p-value= 0.0001, 95%C.I. = 1.70-5.29), social discontinuities was also among the participating factors in the development of gallstones (OR=2.62, p-value= 0.002, 95%C.I. = 1.43-4.79), The geographical mobility factor and catastrophic events appear in this table to do nothing in the occurrence of gallstones.

Table (3) reveals the effect of social context in the occurrence of gallstones, where dramatic change in economic factor, appeared not to be important for a woman to have gallstones. Social integration if not perfect (as living alone), appeared in this study to have no impact in the causation process of gallstones. Urban citizens, in this study appeared to not be more prone to develop gallstones than rural citizens. Lastly, high crowding index again appear to do nothing in the development of gallstones.

Table (2): Distribution of the study population according to life events

Factor	Cases		controls		OR	P-value	95% C.I.
	No.	%	No.	%			
Stress	84	76.36	57	51.82	3.00	0.0001	1.70-5.29
Social discontinuities	42	38.18	21	19.10	2.62	0.002	1.43-4.79
Geographical mobility	10	9.10	18	16.36	0.51	0.106	0.23-1.15
catastrophe	21	19.10	12	10.91	1.93	0.089	0.90-4.12

Table (3): Distribution of the study population according to social context

Factor	Cases		controls		OR	P-value	95% C.I.
	No.	%	No.	%			
Sudden change in job and economic state	10	9.10	11	10	0.90	0.819	0.37-2.21
living alone	1	0.91	1	0.00	1		
Urban	19	17.27	21	19.10	0.89	0.727	0.46-1.71
> 8 persons / household	55	50	52	47.27	1.12	0.686	0.65-1.94

Table (4) indicates that general obesity (BMI > 25) was not valid predictor for the development of gall stones, while central obesity as measured by WHR> 1 appears to be strong risk factor in the development of gallstones (OR=2.18, P-value=0.004, 95% C.I.=1.27-3.73). Unlike chronic diseases, previous history of having typhoid fever emerges as a strapping risk factor in the development of gallstones (OR=3.71, P-value=0.0001, 95% C.I.= 2.13-6.46). Previous abdominal surgeries are not among threats in the occurrence of gall stones. Having more than 4 full term pregnancies appears in this study to be associated with the development of gallstones (OR=3.47, P-value=0.0001, 95% C.I. = 2.01-6.00).

Table (4): Distribution of the study population according to anthropometric measures

Anthropometric measures	cases		controls		OR	P-value	95% C.I.
	No.	%	No.	%			
BMI > 25	47	42.73	48	43.64	0.96	0.892	0.54-1.72
WHR > 1	70	63.63	49	44.55	2.18	0.004	1.27-3.73
Typhoid fever	64	58.18	30	27.27	3.71	0.0001	2.13-6.46
Chronic disease	29	26.36	27	24.55	1.10	0.757	0.60-2.01
Previous abdominal operation	46	41.82	33	30.00	1.68	0.068	0.96-2.93
Parity > 4	68	61.82	35	31.82	3.47	0.0001	2.01-6.00

Discussion:

Gallstones represent a prevalent and costly health problem. Gallstones are now considered as one of the most common digestive diseases; in addition to that, the vast majority of patients who have gallstones are asymptomatic. The changing epidemiology and the emerging non-surgical interventions for gallstone disease necessitate the definition of target populations for future therapies and introducing proper intervention preventive programs.

This study aimed to examine sociological risk factors in the development of gallstones for women at childbearing ages because most of the risk factors are among those clearly related to the lifestyles of the human such as central obesity, unhealthy dietary behaviors, stress and acute changes in role.

Age and gender are important risk factors for the development of gallstones. Gallstones rarely dissolve spontaneously; therefore, their incidence increases with age. Furthermore, most studies report a two to threefold higher risk of gallstone formation in women than in men [3]. This increased incidence is present through the first five decades of life, after which the incidences of gallstones in the sexes equalize. It is believed that estrogens play a role in the increased secretion of cholesterol into the bile in younger women, thus making them more susceptible to the formation of cholesterol stones [12,13]. In this study, the age as a risk factor was beyond measure, because matching of cases and control was based on the factor of age (± 5 years), in addition to that, the gender factor was also immeasurable one, because the study intended to examine sociological risk factors that are related to female gender only (both cases and controls were women in childbearing ages) since, each gender has different behaviors, lifestyles, and expectations especially in eastern Islamic societies where gender difference is still one of main characteristics of those society.

Genetic influence in gallstone formation is suggested by familial clustering within populations. An increased frequency of gallstones was found among the relatives of gallstone patients as compared with families of controls. Familial dietary habits are not likely to offer an explanation of the increased familial incidence of gallstones, in view of the negative findings in spouses. Patients who are young when gallstones develop are more likely to have affected relatives, because an early age onset of gallstone disease would reflect a greater polygenic predisposition. The finding that gallstones are more frequent in monozygotic than in dizygotic twins strongly supported the genetic contribution to gallstone formation [14,15]. In the current study, positive family history was among the significant risk factor in the causation of gallstones for women in childbearing ages.

Sedentary life behaviors, in this work, appeared to be highly associated with gallstones diseases. Regular exercise, in addition to facilitating weight control, alone or in combination with dieting, improves several metabolic abnormalities related to both obesity and cholesterol gallstones. In a prospective study in 60 290 women, increased physical activity was associated with a significant reduction in the risk of cholecystectomy. Not only vigorous physical activities, but also moderate forms of exercise, such as brisk walking, were associated with a reduced risk of cholecystectomy. In contrast, sedentary behaviors, as assessed by time spent sitting, was positively associated with the risk of cholecystectomy [16].

One of the main environmental exposures contributing to gallstone formation is the nutritional exposure. The progressive increase in the prevalence rate of gallstones during this century supports the role of lifestyle and dietary factors in gallstone pathogenesis. Studies in France have observed a higher "caloric intake" in subjects with gallstones than in controls. Refined carbohydrates cause obesity, raise plasma triglyceride and fasting plasma insulin level, and lower plasma HDL cholesterol [17]. A high "fiber intake" in the form of wheat bran lowers the cholesterol saturation of bile. Fibers have a protective effect against cholesterol gallstones by accelerating intestinal transit. The finding of this study was inconsistence with the above facts, where significant difference was observed between cases and control regarding unhealthy dietary behaviors that confirmed it as a strong factor in the causation of gallstones.

Cigarette smoking in this study showed a significant association with gallstones formation. Data related to smoking as a risk factor for gallstones are inconsistent. Some authors found a linear relationship between amount smoked and gallstone risk [18], while other studies found no relation between smoking and gallstones. Smoking is associated with low plasma HDL cholesterol concentrations, a risk factor for gallstones. It also depresses prostaglandin synthesis and mucus production in the gallbladder [18,19].

Some experimental studies have suggested the protective effect of alcohol against gallstone formation as alcohol intake has been shown to reduce bile lithogenicity in humans [19]. The protective effect of alcohol may occur via the liver, by increasing the conversion of cholesterol to bile acids or by altering the enterohepatic circulation of bile acids, including deoxycholic acid, but one cannot suggest alcohol intake because these results were only for moderate intake and the other problems that are associated with alcohol consumption outweigh greatly this minimal benefit. No anyone among both cases and controls in this

research gave positive history of alcohol intake, most probably because this habit is greatly forbidden in our society.

Unlike coronary heart diseases, personality type A, was not associated with the development of gallstones in this work. Moreover, the change in the marital status was not found to be a significant risk factor in the development of gallstone. The same thing was applied for geographical mobility and catastrophic events, where both appeared to be not associated with the occurrence of gallstone diseases. Although these factors are important contributors in the social etiology of diseases, but female gender appeared not to be affected to a big extent by such issues, probably, the domestic responsibilities for women have a role in diminishing the effects of these factors. Urbanization, overcrowding, living alone and sudden change in economic status, all these factors showed insignificant change between cases and controls in this study. Actually, by reviewing literatures, similar studies in evaluation of these factors could not be found.

Stress and stress from social discontinuities, both of them appeared in this work to be associated with gallstones formation. The probable mechanism of action of the stress on the body is that as a causal factor in disease or as a contributory one, by reducing the individual's "resistance" to disease process such as in viral infection or rheumatoid arthritis [9]. The relatively new field of psycho-neuro-immunology, declared the relationship between psychological state, the endocrine system and the body's defense or immune system. Although still characterized by non-specificity, there is evidence that depression and anxiety may adversely affect the immune system and thus increase susceptibility to infections and other illnesses [20].

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. Ultrasonographic and cohort studies in selected populations have confirmed the clinical impression that gallstones are more frequent among obese than non-obese persons [2,21]. Although, in this study, the BMI > 25 appeared not be related in the causation of gallstones, but WHR>1 was a strong risk factor in the development of this disease by about two fold. Obesity, as expressed by BMI>25, in most studies, appeared to be associated with gallstones formation in women rather than in men, but in both gender, WHR>1 emerged as a strong undependable risk factor in the causation of gallstones. Abdominal or central obesity is associated in both men and women with hypertriglyceridaemia, low plasma high-density lipoprotein (HDL) concentrations, impaired glucose tolerance, hyperinsulinaemia etc, and all these metabolic abnormalities are found to be linked with gallstones [21].

Despite general risk factors for most of the chronic non-communicable diseases are similar to that of gallstones formation, no clear association was found in many studies between the presence of these diseases with gallstones [3,7] the same results were obtained from this work. Moreover, the presence of positive history of previous abdominal operations seemed not to be associated with the occurrence of gallstones. Interestingly, positive history of typhoid fever, in this study, increases the risk of gallstone formation by more than three folds, and this may reflects the high rates of infection with salmonella species in our locality.

The influence of the female sex hormones has been examined in normal females, during pregnancy, and in women using oral contraceptives, and the risk of gallstones appeared greater in younger women, and is influenced by parity. A critical review of the literature indicates that parity is associated with gallstones only in younger females. This risk seems to apply to both the number and age of pregnancies. For example, a woman who has four pregnancies before the age of 25 has a fourfold to 12-fold increased risk of cholesterol gallstones compared with an age matched, weight matched nulliparous woman. Pregnancy favors gallstone formation through the hormonal influences on bile composition (increased biliary cholesterol secretion, decreased and unbalanced bile acid pool). This study goes in agreement with the above researches in this topic, where women with more than four pregnancies are found to be at greater risk in the development of gallstones by about 3.5 times.

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