

Association between Gallstones and Diabetics Type 2 Iraqi Patients Anmar H. Altaie*¹

*Department of Pharmacotherapeutics, College of Pharmacy, University of Al-Mustansyria, Baghdad, Iraq

Abstract

Gallstone disease is one of the most common complications among diabetic patients especially type 2 DM. Till now, there is no specific and certain factor that explain the incidence of gallstones among type 2 diabetic patients and many risk factors are taken collectively to estimate its intensity and severity compared to non diabetic counter parts. This clinical study was designed to evaluate and report the incidence and severity of gallstones among type 2 diabetics and non diabetics regarding certain factors. 20 diabetic females and 20 diabetic males were collected as patients' group and have had gallstones while 20 females and 20 males who have had gallstones without diabetes mellitus type 2 were collected as controls' group. The age, weight, and both of the size and number of gallstones of diabetic patients and controls were correlated to demonstrate the prevalence of gallstones among the patients' and controls' groups. The study showed that the mean ages of female patients is slightly higher ($p < 0.05$) than the female controls. On the other hand there was a significant difference ($p < 0.05$) between female and male control subjects. The body mass index (BMI) of male patients was significantly higher ($p < 0.05$) than the male controls, while there was a significant difference ($p < 0.05$) between female and male control subjects. The results of the study presented that the stone size of female patients was significantly higher ($p < 0.05$) than the female and male controls, while the stone diameter of male patients was significantly higher ($p < 0.05$) than the male and female controls. The stone number of female patients was significantly higher ($p < 0.05$) than the female and male controls, while the stone number of male patients was significantly higher ($p < 0.05$) than the male and female controls. These findings suggest that the incidence of gallstones was higher in type 2 diabetics both in males and females than the non diabetics and more in females than males who were non diabetics.

Key words: Diabetes mellitus, gallstones, gender, ultrasound

الخلاصة

مرض حصي المرارة أحد أكثر التعقيدات بين المرضى بداء السكري خصوصاً النوع الثاني. حتى الآن، ليس هناك عامل معين ومُتأكد الذي يوضحُ حادثة حصي المرارة بين المرضى بداء السكري خصوصاً النوع الثاني وإن العوامل مأخوذة بشكل جماعي لتخمين كثافته وشِدته بين المرضى بداء السكري خصوصاً النوع الثاني وغير المصابين بداء السكري. هذه الدراسة السريرية صُممت للتقييم وتقييم شدة حصي المرارة بين المرضى بداء السكري خصوصاً النوع الثاني وغير المصابين بداء السكري. 20 من الإناث مريضات بداء السكري من النوع الثاني و20 من الذكور مرضى بداء السكري من النوع الثاني أيضاً، جمعوا كعينة مرضى وكانوا مصابين بحصي المرارة بينما 20 من الإناث و20 من الذكور جمعوا كعينة وتم فحصهم مختبرياً للتأكد من عدم إصابتهم بالسكري وكان عندهم حصي المرارة فقط. عُمر ووزن المرضى وحجم وعدد حصي المرارة للمرضى المصابين بداء السكري من النوع الثاني وغير المصابين به أظهرت الدراسة بأن متوسط الأعمار للمرضى الإناث أعلى قليلاً من متوسط الأعمار ($p < 0.05$) للإناث الذين أخذوا كعينة من الناحية الأخرى كان هناك اختلاف هام ($p < 0.05$) بين متوسط الأعمار للذكور والإناث الذين أخذوا كعينة. إن دليل كتلة الجسم (بي. ام. اي) من المرضى الذكور أعلى جداً ($p < 0.05$) من الذكور (الذين أخذوا كعينة)، بينما كان هناك اختلاف هام ($p < 0.05$) بين دليل كتلة الجسم (بي. ام. اي) للذكور والإناث الذين أخذوا كعينة. وضحت نتائج الدراسة حجم حصي المرارة للمرضى الإناث أعلى جداً ($p < 0.05$) لدى الإناث والذكور الذين أخذوا كعينة، بينما قطر حصي المرارة لدى المرضى الذكور أعلى جداً ($p < 0.05$) من الذكور والإناث الذين أخذوا كعينة. إن عدد حصي المرارة لدى المرضى الإناث أعلى جداً ($p < 0.05$) من الذكور والإناث الذين أخذوا كعينة، بينما إن عدد حصي المرارة لدى المرضى الذكور أعلى جداً ($p < 0.05$) من الذكور والإناث الذين أخذوا كعينة. تقررُ هذه النتائج بأن حادثة حصي المرارة أعلى لدى المصابين بداء السكري من النوع الثاني في كلا في الذكور والإناث وكذلك أعلى في الإناث من الذكور من المصابين بحصي المرارة وغير مصابين بداء السكري.

Introduction

Diabetes is a chronic condition caused by a relative or an absolute lack of insulin⁽¹⁾. It is associated with abnormalities in carbohydrate, fat, and protein metabolism and results in chronic complications including microvascular, macrovascular, and neuropathic disorders⁽²⁾. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and life-style

choices. The two broad categories of DM are designated type 1 and type 2⁽³⁾. Gallstones (chole = "bile", lithia = "stone", and -sis = "process") are the most common digestive disease causing huge hospitalizations annually worldwide⁽⁴⁾. Gallstones can occur anywhere within the biliary tree, including the gallbladder and the common bile duct⁽⁵⁾.

1Corresponding author E- mail : altai1978@yahoo.com

Received : 12/5/2011

Accepted : 8/10/2011

Gallstones are formed by concretion or accretion of normal or abnormal bile constituents. They are divided into two major types: cholesterol stones account for 80% of the total, with pigment stones comprising the remaining 20%⁽³⁾. Gallstones can occur at any age, although they are rare under the age of 10 years and most common at 50–60 years in both sexes. Women are more prone to develop gallstones than men⁽⁶⁾. There are several factors which directly affect the formation of gallstones as; sex, age, obesity, diet with high calories, diabetes mellitus, hemolytic anemia, estrogen and clofibrate therapy etc.^(7,8,9). Diabetic subjects are reported to have a two to three fold increase in the prevalence of cholesterol gallstone. Inadequate emptying of gallbladder and increased fasting gallbladder volume has been reported in various studies⁽¹⁰⁾. In the present study, the incidence of gallstones in type 2 diabetics is made in correlation with age, sex and weight, the size and number of stones were taken in consideration.

Materials and Methods

This study was carried out on (80) patients. Of those 40 subjects (20 males, 20 females) have gallstones without diabetes mellitus type 2 served as a control group and 40 patients (20 males, 20 females) have diabetes mellitus type 2 with gallstones. Certain exclusion criteria were followed to avoid interference of any other factors like drugs or pathological conditions with this research, which include: patients with history of gallstones and received previous therapy or undergoing treatment, patients with history of clinical disorders like hyperlipidemia, hepatic disorders and those taking medications other

than prescribed for DM type 2. Those patients were diagnosed and treated in Al-yarmook Teaching Hospital under supervision of specialist physicians. Type 2 diabetic patients were diagnosed and selected based on American Diabetes Association criteria of DM (2004): fasting plasma glucose concentration ≥ 126 mg/dl, 2hr postprandial glucose concentration ≥ 200 mg/dl and whose age at the onset of type 2 DM was equal or greater than 40 years. Gallstones identification, size and number were determined by ultrasonography which is thought to be the most appropriate technique in the diagnosis of the gallstones.

Statistical Analysis

The results were expressed as mean \pm SD, student t-test and ANOVA test were used to examine the degree of significance which is considered significant as P value <0.05 .

Results

Both of table 1 and figure 1, show the age distribution of patients depending on their gender. The mean ages of female patients having gallstones and DM type 2 was (56.2 \pm 9.24) years, is slightly higher ($p<0.05$) than the female controls having gallstones without diabetes (49.5 \pm 10.62) years while the mean ages of male patients having gallstones and DM type 2 was (58 \pm 10.5) years is significantly indifferent ($p<0.05$) from the male controls having gallstones without diabetes (58.2 \pm 10.88) years. On the other hand there was a significant difference ($p<0.05$) in the mean age between female and male control subjects (49.5 \pm 10.62), (59.58 \pm 10.5) years old respectively.

Table 1: Characteristics of study parameters for both control subjects (having gallstones without type 2 DM) and patient subjects (having gallstones and type 2 DM)

Type and no. of patients	Age (year) mean \pm SD	BMI kg/m ² mean \pm SD	Gallstones' size (mm) mean \pm SD	Gallstones' number mean \pm SD
Non diabetic females(20)	49.5 \pm 10.62	27.217 \pm 2.96#	3.37 \pm 1.31	3.0 \pm 1.0
Diabetic females(20)	56.2 \pm 9.24*	27.218 \pm 2.6#	7.49 \pm 4.35*#	5.0 \pm 3.0*#
Non diabetic males(20)	58.2 \pm 10.88#	25.05 \pm 2.78	3.36 \pm 1.63	2.0 \pm 1.0
Diabetic males(20)	58.2 \pm 10.88#	28.48 \pm 2.57*	6.4 \pm 3.48*#	5.0 \pm 3.0*#

*Significantly different from control ($p<0.05$).

Significantly different between groups ($p<0.05$)

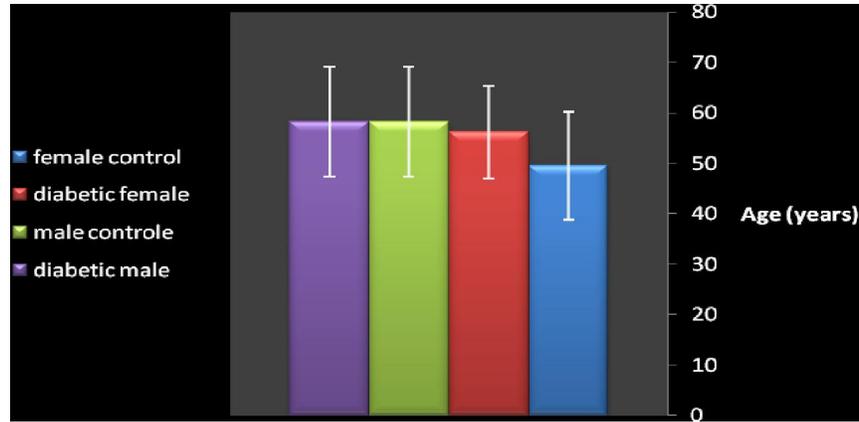


Figure 1: The mean age of both control subjects (having gallstones without type 2 DM) and patient subjects(having gallstones and type 2 DM)

As presented in table 1 and figure 2, the body mass index (BMI) of female patients having gallstones and type 2 DM (27.218 ± 2.6) kg/ m² was significantly indifferent ($p < 0.05$) than the female controls (27.217 ± 2.96) kg/ m², while the BMI of male patients having gallstones and DM type 2 (28.48 ± 2.57) kg/ m² was significantly higher ($p < 0.05$) than the male controls (25.05 ± 2.78) kg/ m². On the other hand there was a significant difference ($p < 0.05$) between female and male controls (27.218 ± 2.6), (25.05 ± 2.78) kg/ m² respectively ,and between female patients (27.217 ± 2.96) kg/ m² and male control (25.05 ± 2.78) kg/ m². The stone diameter of female patients having gallstones and DM type 2 was (7.49 ± 4.35)mm is significantly higher ($p < 0.05$) than the female and male controls having gallstones without diabetes

(3.37 ± 1.31), (3.36 ± 1.63) mm respectively, while the stone diameter of male patients having gallstones and DM type 2 was (6.4 ± 3.48) mm, is significantly higher ($p < 0.05$) than the male and female controls having gallstones without diabetes was (3.36 ± 1.63), (3.37 ± 1.31) mm ,respectively as shown in both of table 1 and figure 3. Table 1 and figure 4, also present that the stone number of female patients having gallstones and DM type 2 was (5.0 ± 3.0), is significantly higher ($p < 0.05$) than the female and male controls having gallstones without diabetes (3.0 ± 1.0) (2.0 ± 1.0) respectively, while the stone number of male patients having gallstones and DM type 2 was (5.0 ± 3.0), is significantly higher ($p < 0.05$) than the male and female controls having gallstones without diabetes (2.0 ± 1.0), (3.0 ± 1.0) respectively.



Figure 2: The BMI(kg/ m²) of both control subjects (having gallstones without type 2 DM) and patient subjects(having gallstones and type 2 DM)

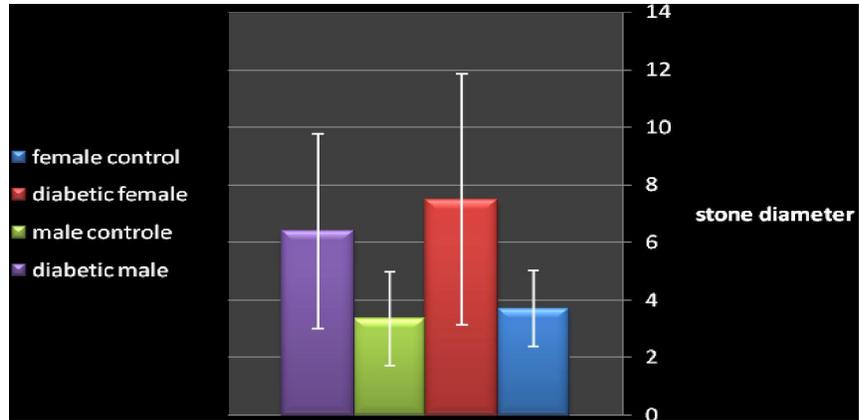


Figure 3: The gallstone diameter(mm) of both control subjects (having gallstones without type 2 DM) and patient subjects(having gallstones and type 2 DM)

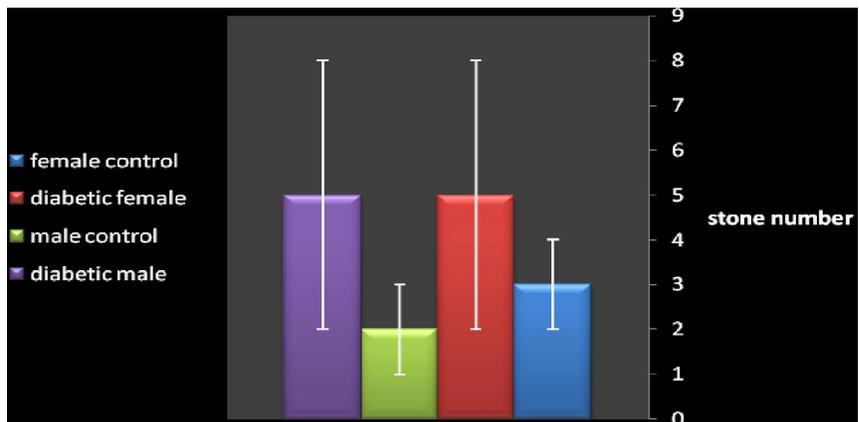


Figure 4: The gallstone number of both control subjects (having gallstones without type 2 DM) and patient subjects(having gallstones and type 2 DM)

Discussion

Gallstone disease is one of the most common digestive diseases⁽⁴⁾. Many studies investigate and demonstrate the relationship between gallstones and type 2 DM. Ali Ekecik et al⁽¹¹⁾ reported a statically significant difference ($p < 0.01$) in the frequency of gallstones between 200 non diabetic control group and 200 diabetic patients, the incidence was 10.5%(21/200) in the control group versus 27%(54/200) in type 2 diabetic patients. One of the risk factors for cholesterol gallstones includes increasing age and female gender. In the present study as showed in table 1, the age of the patients regarding the gender plays a great role in the incidence of gallstones in that the incidence was significantly higher between female and male control subjects. On the other hand there was a significant difference ($p < 0.05$) among females having

type 2 diabetes than the controls, while age plays non-significant role in the incidence of gallstones among type 2 diabetic males than the controls. The incidence was insignificantly higher between female and male patients having type 2 DM suggesting the role of factors other than the relationship between age and gender. The mean age of onset of gallstones among both the control and patient females was totally lower than the mean age of both the control and patient males. This finding may be attributed to the fact that females are reported to have prevalence of gallstones till the age of 50 probably due to hormonal influence on bile composition and gallbladder motility⁽¹²⁾. The results of this study is in harmony with that done by Rupali Saxena et al⁽¹²⁾, who found that 67.5% of the diabetic patients with gallbladder disorder

were females, as well as by Sun H. et al⁽¹³⁾ who stated that the incidence of gallstone was higher in females than in males and with increasing age 40-64 or ≥ 65 years, while Champan et al⁽¹⁴⁾ stated that subjects of both sexes with type 2 DM, had higher prevalence of gallstones than controls. Another risk factor for the increased incidence of gallstones in type 2 diabetics is obesity. Table 1 shows the effect of body weight regarding gender on the incidence of gallstones where the incidence was significantly higher between female and male control subjects, while insignificant between female and male diabetic patients but again significantly different between male patients having gallstones and type 2 DM and control males. The results of this study agree with a study done by A. B. Olokoba et al⁽¹⁵⁾ who founded that the diabetic patients had a significantly higher mean BMI than the controls ($P < 0.01$) in 100 type 2 diabetic patients and 100 age- and sex-matched controls. But again obesity alone is independent risk factor among obese type 2 diabetic patients and a number of factors are collectively responsible for the increasing incidence of gallstones and type 2 DM. In diabetics, lipid concentration of plasma and bile increase. The obesity observed in diabetic patients has diverse effects on increased cholesterol synthesis and bile saturation^(16,17) Additionally, in the obese, gallbladders may not empty normally or completely⁽¹⁸⁾. As BMI increases, the risk for developing gallstones also rises. For women, obesity is an even stronger risk factor for developing gallstones and women with a BMI greater than 32 may be as much as three times as likely to develop gallstones as those with a BMI of 24 or 25. The risk may be seven times higher in women with a BMI above 45 than in those with a BMI under 24⁽¹⁹⁾, and this may explain why there was insignificant difference between the control and the diabetic females. The last two parameters are the gallbladder stones' sizes and numbers and their associated incidence among controls and type 2 diabetic patients. Both of the size and number of gallstones were significantly higher in female and male patients than in the both sexes of the controls. The supersaturation of bile with cholesterol, nucleation of monohydrate crystals and dysfunction of gall bladder are the three important factors that cause gallstone formation^(20,21). Hypomotility of gallbladder cause gallstone formation in diabetes mellitus and other chronic disorder like obesity⁽²²⁾. The gallbladder of diabetic patients are generally large and its motility is disturbed⁽²³⁾. These

events are probably due to the dysfunction of the gall bladder wall. The combined effects of poor emptying and possibly decreased ejection fraction rate and increased fasting volume could lead to bile stasis within the gallbladder and the formation of stones⁽²⁴⁾.

Conclusions

From the results and discussion of this study, we conclude that the incidence of gallstones is higher in type 2 diabetics both in males and females than the non diabetics and more in females than males who are non diabetics and multiple factors collectively are associated with this incidence that ultimately lead to marked increase in stone size and number.

References

1. Lisa A. Kroon, MitraAssemi, Betsy A. Carlisle. Diabetes Mellitus. In: Applied therapeutics the clinical use of drugs. Mary annekoda-kimble, Lioyd Yee Young, Brian K. Alldredge, et al. 9th Ed., Lippincot. USA. 2009, p50-53.
2. Stephan ND, Daryl KG. Insulin, oral hypoglycaemic agents, and the pharmacology of the endocrine pancreas. In: Goodman and Gilman's The Pharmacological basis of Therapeutics. Hardman JG, Limbird LE editors. 10th Ed. New York: McGraw- Hill. USA. 2001, p. 1686-7.
3. Alvin C. Powers. Diabetes Mellitus. In: Harrison's principles of Internal Medicine. Dennis L. Kasper, Eugene Braunwald, Anthony S. Fauci, et al. 16th Ed. McGraw-Hill Medical Publishing Division. USA. 2005, p. 2152.
4. Portincasa P, Moschetta A, Palasciano G. Cholesterol gallstone disease. The Lancet 2006;368(9531):230-39.
5. Suita S, Ikeda K, Naito K, Doki T, Handa N. Cholelithiasis in Infants: Association with Parenteral Nutrition. Journal of Parenteral and Enteral Nutrition. 1984;8(5):568-70.
6. Russell J Greene, Norman D Harris. In :Pathology and therapeutics for pharmacists. 3rd Ed. Pharmaceutical Press. UK. 2008. p 150.
7. .Menteş NK. Klinikgastroenteroloji. GüvenKitabeviizmir. 1983; 2; 810-8.
8. Şimşek H, Tatar G, Kayhan B, et al. SafraTaşlarıveTıbbiTedavisi (Medical management of gallstones). TürkilaçveTedaviDergisi. 1990; 3(3): 433-40.
9. Tanno N, Koizumi M. The relationship

- between cholelithiasis and diabetes mellitus; discussion of age, obesity, hiperlipirdemia and neuropathy. *Tohoku J. Exp. Med.* 1988; 154: 11-20.
10. Gitelson, S., Schwart, A., Frankel, M., Chowers, et al . Gallbladder dysfunction in diabetes mellitus: the diabetic neurogenic gallbladder. *Diabetes.* 1963; 12: 308-12.
 11. Ali EKECİK1 , Saniye TOPÇU1 , Mübeccel A K S U 2 ,et al. Frequency of gallstones in diabetes mellitus. *Turk J Med Res.* 1994; 12(2):87-90]
 12. Rupali Saxena1, Sunita Sharma1 and D.C. Dubey. Gallbladder Disorder in Type 2 Diabetes Mellitus Cases. *J. Hum. Ecol.* 2005; 18(3): 169-171.
 13. Hui Sun, Hong Tang, Shan Jiang, et al. Gender and metabolic differences of gallstone diseases. *World J Gastroenterol.* 2009; 41(15): 1886-1891.
 14. Chapma BA, Wilson IR, Frampton CM. Prevalence of gallbladder disease in diabetes mellitus. *Digestive Diseases and Sciences.* 1996; 41(11): 2222 – 2228.
 15. A. B. Olokoba, B. J. Bojuwoye, I. A. Katibi,et al. The effect of type 2 diabetes mellitus on fasting gallbladder. *African Scientist.* 2006. 7(3), 117-120.
 16. Feldman M, Feldman M Jr et al. Incidence of cholelithiasis, cholesterosis and liver disease in diabetes mellitus, autopsy study. *Diabetes.* 1954;23: 305-12.
 17. Hozbach RT. Pathogenesis and medical treatment of gallstones. In: Sleisenger MH, Fordtan J S , eds. *Gastrointestinal Disease*, 4thEd. WB saunders. Philadelphia,USA. 1989, p 1668-90.
 18. *The Health Risks of Obesity: Obesity and Gallstones.* By Jennifer R. Scott, About.com Guide Updated January 15, 2009.
 19. *Dieting and Gallstones.* National Institute of Diabetes and digestive and kidney diseases.
 20. Paumgartner T, Sauerbruch T. Gallstones: Pathogenesis, *The Lancet*, 1991; 8777:1117-21.
 21. Sherlock K, Dooley J. Diseases of the liver and biliary system. In: *Gastrointestinal disease.* SleisengerMH, FordtranJS, editors. Blackwell scientific publications. UK. 1993;p. 562-92.
 22. Hahm, J.S., Park, J.Y., Song, S.C. et al. Gallbladder motility change in late pregnancy and after delivery. *Korean J. Intern.Med.* 1997; 12:16-20.
 23. Blomm AA, Stochengeld R. Diabetic cholecystomegaly. *JAMA.* 1985;408:357-9.
 24. Takahashi T, Yamamura T, Yokoyama E, et al. Impaired contractile motility of the gallbladder after gastrectomy. *Am J Gastroenterol.* 1986; 81: 672-77