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Factors conditioning severity of grade I vs. grade II cholecystitis in adult women

Factores que condicionan severidad de colecistitis grado I vs. grado II en mujeres adultas

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ABSTRACT

Introduction: Cholelithiasis is a public health problem in Mexico. Obesity is considered a risk factor for the development of this disease; however, its role in influencing the severity of cholecystitis is not well defined. **Objective:** To evaluate the factors that condition the severity of cholecystitis (grade I vs. grade II, according to the Tokyo 18 guidelines) in women in a public hospital in Ciudad Juarez, Mexico. **Material and methods:** Cross-sectional study in women with grade I and II cholecystitis who underwent laparoscopic cholecystectomy. The following parameters were assessed and compared: age, weight, height, body mass index (BMI), waist, hip, waist-to-hip ratio (WHR), blood pressure, glucose, cholesterol, high-density lipoprotein-cholesterol (HDL), triglyceride levels, white blood cell count, neutrophil count, surgical time, and presence of type 2 diabetes (DM2), high blood pressure (HBP), hypertriglyceridemia, hypercholesterolemia, dyslipidemia, abdominal obesity, WHR obesity, and metabolic syndrome (MS). **Results:** 132 patients were included in this study and only statistically and clinically significant differences were observed in the mean triglyceride levels (155.9 vs. 178.4; p = 0.008), and in the presence of hypertriglyceridemia (40.5% vs. 70.8%; p = 0.001). **Conclusions:** Obesity measured by BMI, waist and/or WHR do not seem to be related to the degree of severity of cholecystitis (grade I vs. grade II), while mean triglyceride levels and the presence of hypertriglyceridemia may act as aggravating factors in acute grade II cholecystitis.

RESUMEN

Introducción: *La colelitiasis es un problema de salud pública en México. La obesidad se considera un factor de riesgo de la génesis de esta enfermedad; sin embargo, no está bien definido su papel con respecto a la influencia en la severidad del cuadro de colecistitis.* ***Objetivo:*** *Evaluar los factores que condicionan la severidad en un cuadro de colecistitis (grado I vs. grado II, según las guías de Tokio 18) en mujeres en un hospital público en Ciudad Juárez.* ***Material y métodos:*** *Estudio transversal en mujeres con colecistitis grado I y II sometidas a colecistectomía laparoscópica. Se evaluaron y compararon las siguientes variables: edad, peso, talla, índice de masa corporal (IMC), cintura, cadera, índice cintura/cadera (ICC), tensión arterial, glucosa, colesterol, lipoproteínas de alta densidad (HDL), triglicéridos, leucocitos, neutrófilos, tiempo quirúrgico, presencia de diabetes tipo 2 (DM2), hipertensión arterial (HTA), hipertrigliceridemia, hipercolesterolemia, dislipidemia, obesidad abdominal, obesidad por ICC y síndrome metabólico (SM).* ***Resultados:*** *Se estudiaron 132 pacientes, sólo se observó diferencia estadísticamente significativa y significancia clínica en el promedio de triglicéridos (155.9 vs. 178.4; p = 0.008), y en la presencia de hipertrigliceridemia (40.5% vs. 70.8%; p = 0.001).* ***Conclusiones:*** *La obesidad medida por el IMC, cintura y/o ICC no parecen tener relación con el grado de severidad de la colecistitis (grado I vs. grado II), mientras que el promedio de triglicéridos y la presencia de hipertrigliceridemia sí pueden actuar como factores agravantes de la colecistitis aguda grado II.*

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INTRODUCTION

Nowadays, cholelithiasis is a public health problem.[1] Necropsy studies reveal that 12% of men and 24% of women suffer from this entity.[2] Although 80% of patients with cholelithiasis may remain asymptomatic, the rest present with symptoms such as biliary colic, and complications such as cholecystitis, choledocholithiasis, pancreatitis, and cholangitis, among others.[2]

The risk factors for cholelithiasis and cholecystitis are well defined. While obesity is classically considered as an etiologic factor, central obesity, and waist-to-hip ratio (WHR) are suggested to play an important role in the severity of cholecystitis.[3]

The aim of this study is to evaluate which factors may condition the occurrence of grade II cholecystitis in a female population undergoing laparoscopic cholecystectomy.

MATERIAL AND METHODS

From January through December 2018 a cross-sectional study was performed at the General Hospital de Zona No. 35 of the Mexican Social Security Institute (HGZ No. 35, IMSS) in Ciudad Juarez, Mexico. Female patients aged 18 to 65 years, admitted to hospital with a diagnosis of acute cholecystitis and who underwent laparoscopic cholecystectomy were included.

Patients with liver diseases such as cirrhosis, cysts or liver tumors of any etiology, cancer of the rest of the digestive tract, pregnancy, and patients whose cholecystectomy had been converted from laparoscopic to open cholecystectomy were excluded.

The patients were divided into two groups: group 1 included patients with acute cholecystitis without any other complication or grade I cholecystitis, and group 2 included patients with complicated acute cholecystitis (choledocholithiasis, cholangitis, biliary pancreatitis, mucocele, empyema, etc.) without any organic dysfunction or grade II. The diagnosis of acute cholecystitis, as well as the differentiation between grade I and grade II acute cholecystitis, was determined based on the operative findings and the criteria of the Tokyo 18 guidelines *(Tables 1 and 2)*.[4]

Laparoscopic cholecystectomy was performed as a treatment for acute cholecystitis. The operation was performed by the same surgical team using the standard four-port technique.[5] The procedure was performed during the same hospitalization period.

Following parameters were measured: age, weight, height, body mass index (BMI), waist, hip, waist-to-hip ratio (WHR), blood pressure, glucose, cholesterol, high-density lipoprotein-cholesterol (HDL-C), triglycerides, white blood cells, neutrophils, surgical time, and presence of type-2 diabetes (DM2), high blood pressure (HBP), hypertriglyceridemia (≥ 150 mg/dl), hypercholesterolemia (≥ 200 mg/dl), dyslipidemia (altered cholesterol and/or triglycerides), abdominal obesity (hip 88 cm), waist-to-hip ratio (WHR) obesity (≥ 0. 85), and metabolic syndrome (MS).

Weight and height were measured with the patient barefoot and wearing a hospital gown, BMI was calculated by dividing weight (kg) by height squared (meters). Waist and hip circumference were measured with a flexible tape measure with the patient in fasting state,

Table 1: Diagnostic criteria for acute cholecystitis according to the Tokyo 18 guidelines.

A. Local signs of inflammation
1. Murphy's sign
2. Pain/mass/tenderness in URQ
B. Signs of systemic inflammation
1. Fever
2. CPR increased
3. White blood cell counts increased
C. Image study findings
Characteristic findings of acute cholecystitis*
Diagnostic suspicion:
one element of A + one element of B
Definitive diagnosis:
one element of A + one element of B + C

URQ = upper right quadrant; CPR = C-reactive protein.
* Imaging findings: thickening of the vesicular wall, peri-vesicular fluid, positive Murphy's sonographic sign.

Table 2: Severity criteria for acute cholecystitis according to the Tokyo 18 guidelines.

Grade III (severe)
Acute cholecystitis associated with dysfunction of any of the following organs/systems:
1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 μg/kg per minute or epinephrine at any dose
2. Neurological dysfunction: alteration of consciousness
3. Respiratory dysfunction: PaO_2/FiO_2 ratio < 300
4. Renal dysfunction: oliguria, creatinine > 2.0 mg/dl
5. Hepatic dysfunction: PT-INR > 1.5
6. Hematologic dysfunction: platelet count < 100,000/mm^3

Grade II (moderate)
Acute cholecystitis associated with any of the following conditions:
1. Leukocytosis > 18,000/mm^3
2. Palpable mass in the right upper quadrant
3. Duration of symptoms > 72 h
4. Marked local inflammation (gangrene, peri-vesicular or hepatic abscess, emphysema, empyema, mucocele, etc.)

Grade I (mild)
Acute cholecystitis that does not meet criteria for grade III or II. It can also be defined as acute cholecystitis in a previously healthy patient, without organ dysfunction or moderate inflammatory changes in the gallbladder, and whose cholecystectomy is performed safely and with low operative risk

PT = prothrombin time, INR = International Normalized Ratio.

always in the standing position, and the tape placed at the level of the navel for the waist and at the level of the most prominent gluteal part for the hip.

Since no experimental intervention was performed, this study did not require approval by the institutional bioethics committee if the patients' informed consent for the surgical procedure was already obtained.

Statistical analyses of the parameters were performed with the SPSS program (version 23.0; Chicago, Il). Qualitative variables were compared with the χ^2 test, and quantitative variables with Student's t test (normal behavior variables) and the Mann-Whitney U test (abnormal behavior variables). A p value < 0.05 was considered statistically significant.

RESULTS

We evaluated 132 patients who met the inclusion criteria, with a mean age of 38.6 years, a mean BMI 31.8 kg/m^2, and a mean triglyceride level of 164 mg/dl; the rest of the parameter values are shown in *Table 3*.

Table 3: Numerical characteristics of the total number of patients studied.

Parameter	Mean ± SD	Minimum	Maximum
Age (years)	38.6 ± 10.6	20	69
Weight (kg)	77.4 ± 15.4	45	115
Height (cm)	156.0 ± 6.2	140	173
BMI (kg/m^2)	31.8 ± 6.1	18.7	48.5
Waist (cm)	101.1 ± 13.7	67	130
Hip (cm)	110.7 ± 12.3	80	145
WHR	0.9 ± 0.1	0.72	1.09
Systolic blood pressure (mmHg)	118.6 ± 17.2	90	180
Diastolic blood pressure (mmHg)	74.7 ± 11.8	50	110
Glucose (mg/dl)	104.2 ± 32.6	70	344
Cholesterol (mg/dl)	186.8 ± 48.4	84	407
HDL-cholesterol (mg/dl)	40.7 ± 9.8	22	67
Triglycerides (mg/dl)	164.1 ± 75.5	47	505
White blood cells (× 10^9/l)	10.4 ± 10.1	4	18
Neutrophile count (%)	67.3 ± 13.6	39	97
Surgical time (minutes)	64.5 ± 27.3	30	200

SD = standard deviation; BMI = body mass index; WHR = waist-to-hip ratio; HDL-cholesterol = high-density lipoprotein cholesterol.
Source: archive of the HGZ No. 35, IMSS.

Table 4: Comorbidities in the total number of patients.

Parameter	Total of patients (N = 132) n	%
DM2		
No	80	60.6
Yes	52	39.4
HBP		
No	120	90.9
Yes	12	9.1
Hipertriglyceridemia		
No	64	48.5
Yes	68	51.5
Hypercholesterolemia		
No	89	67.4
Yes	43	32.6
Dyslipidemia		
No	52	39.4
Yes	80	60.6
BMI		
Normal weight	18	13.6
Overweight	32	24.2
Obesity	82	62.1
Abdominal obesity		
No	23	17.4
Yes	109	82.6
WHR obesity		
No	23	17.4
Yes	109	82.6
MS		
No	59	44.7
Yes	73	55.3

DM2 = type 2 diabetes mellitus; HBP = high blood pressure; BMI = body mass index; WHR = waist-to-hip ratio; MS = metabolic syndrome.
Source: archive of the HGZ No. 35, IMSS.

Regarding the comorbidities presented in the total number of patients, we found a prevalence of DM2 of 39.4%, HBP of 9.1%, hypertriglyceridemia of 51.5%, among others. The remaining percentages are described in *Table 4*.

Quantitative variables were compared by groups (grade I vs. grade II) and statistically significant differences were observed in the mean triglyceride levels, and in white blood cell and neutrophil counts. The rest of the values that were not statistically significant are shown in *Table 5*.

Regarding comorbidities between the groups, a statistically significant difference was seen in the presence of hypertriglyceridemia and dyslipidemia. The rest of the comorbidities that were not statistically significant are detailed in *Table 6*.

DISCUSSION

Acute cholecystitis is the most common complication of cholelithiasis, with a mortality of approximately 3%. The standard treatment is laparoscopic cholecystectomy;[6] however, open cholecystectomy continues to be performed in some second level care centers.[7]

Overweight and obesity increase the risk of cholelithiasis[8] through the increased secretion of cholesterol in the liver, which produces supersaturation and precipitation of bile with the consequent formation of calculi. The role of obesity in the development of gallstones is clear, but its role is debatable with respect to its severity. The presence of obesity in the context of cholelithiasis implies a chronic visceral inflammatory state that could influence the severity of acute cholecystitis. However, in this study the means between groups (grade I vs. grade II) were not statistically significant in relation to BMI, waist, hip, and WHR. This could suggest that, although obesity predisposes to a visceral inflammatory state at the onset of the disease, once cholecystitis is established, obesity per se does not seem to influence the severity of the condition.

Although the relationship between serum total cholesterol levels and the frequency of cholelithiasis has not been demonstrated, we were able to observe that both the mean triglyceride levels (155.9 vs. 178.4 mg/dl; p = 0.008) and the presence of hypertriglyceridemia (40.5% vs. 70.8% mg/dl; p = 0.001) were correlated with group 2 (grade II cholecystitis). Alterations in lipid metabolism are a pivotal element in the development of cholelithiasis in patients with obesity. This duality is characterized

Table 5: Numerical characteristics of the studied groups.

Parameter	Group 1 (n = 84) Mean ± SD	Group 2 (n = 48) Mean ± SD	p value
Age (years)	39.1 ± 10.3	37.7 ± 11.0	0.48*
Weight (kg)	77.2 ± 16.6	77.6 ± 13.1	0.88*
Height (cm)	156.3 ± 6.3	155.4 ± 6.2	0.42*
BMI (kg/m^2)	31.6 ± 6.6	32.1 ± 5.2	0.61*
Waist (cm)	100 ± 13.7	103.1 ± 13.7	0.21*
HIP (cm)	110.1 ± 13.0	111.7 ± 11.0	0.48*
WHR	0.9 ± 0.1	0.9 ± 0.1	0.23*
Systolic blood pressure (mmHg)	118.8 ± 17.8	118.3 ± 16.1	0.87*
Diastolic blood pressure (mmHg)	75.1 ± 11.9	74 ± 11.7	0.61*
Glucose (mg/dl)	101.8 ± 24.6	108.3 ± 43.1	0.26*
Cholesterol (mg/dl)	183.2 ± 48.9	193.1 ± 47.3	0.26*
HDL-cholesterol (mg/dl)	41.8 ± 9.8	38.6 ± 9.7	0.06**
Triglycerides (mg/dl)	155.9 ± 81.6	178.4 ± 61.6	0.008**
White blood cells (× 10^9/l)	9.7 ± 12.2	11.6 ± 4.3	< 0.01**
Neutrophils (%)	63.1 ± 12.6	74.8 ± 12.0	< 0.01*
Surgical time (minutes)	61.4 ± 20.2	69.9 ± 36.1	0.14*

* Student-t test; ** Mann-Whitney U test.
SD = standard deviation; BMI = body mass index; WHR = waist-to-hip ratio; HDL-cholesterol = high density lipoprotein cholesterol.
Source: Archive of the HGZ No. 35, IMSS.

by hypertriglyceridemia that correlates with lack of gallbladder motility[9] being therefore a factor in the development of cholelithiasis. The results of this study suggest that elevated triglyceride levels do significantly increase the risk of severity (at least to grade II), which would condition both an aggravation of the disease and act as a risk factor for severity.

Other studies have suggested that obesity may be a protective factor against the severity of cholelithiasis in male patients, and that visceral fat may have a protective function against the inflammatory state in cholecystitis.[8] These same results have not been reproduced in other studies.[10,11] Cholelithiasis has a direct relationship with non-alcoholic grade liver,[12] and fatty infiltration in visceral organs such as the liver can cause chronic inflammation, so the assumption that visceral fat conditions protection could be contradictory.[13]

DM2 and HBP are considered risk factors for developing acute cholecystitis.[14] Fagan et al. demonstrated that DM2 did influence the development of gangrenous cholecystitis.[15] However, our results suggest that both DM2 and HBP appear not to influence the development of complications. This has been a subject to discussion and larger studies are required to corroborate the true role of these comorbidities in the severity of cholecystitis.

CONCLUSION

In the present study, the results suggest that high triglyceride levels could act as a risk factor for grade II cholecystitis. No relationship was demonstrated between obesity measured by BMI, waist, hip and/or WHR with the severity of cholecystitis (grade I vs. grade II). However, more prospective, or multicenter studies are needed to corroborate these findings.

Table 6: Comorbidities of study patients.

Parameter	Group 1 (n = 84) n	Group 1 (n = 84) %	Group 2 (n = 48) n	Group 2 (n = 48) %	p*
DM2					
No	50	59.5	30	62.5	0.73
Yes	34	40.5	18	37.5	
HBP					
No	77	91.7	43	89.6	0.68
Yes	7	8.3	5	10.4	
Hypertriglyceridemia					
No	50	59.5	14	29.2	0.001
Yes	34	40.5	34	70.8	
Hypercholesterolemia					
No	57	67.9	32	66.7	0.88
Yes	27	32.1	16	33.3	
HDL-cholesterol (< 50 mg/dl)					
No	19	22.6	7	14.6	0.26
Yes	65	77.4	41	85.4	
Dyslipidemia					
No	41	48.8	11	22.9	0.003
Yes	43	51.2	37	77.1	
BMI					
Normal weight	14	16.7	4	8.3	0.24
Overweight	22	26.2	10	20.8	
Obesity	48	57.1	34	70.8	
BMI					
< 30	34	40.5	14	29.2	0.19
≥ 30	50	59.5	34	70.8	
Abdominal obesity					
No	15	17.9	8	16.7	0.86
Yes	69	82.1	40	83.3	
WHR obesity					
No	17	20.2	6	12.5	0.26
Yes	67	79.8	42	87.5	
MS					
No	42	50.0	17	35.4	0.1
Yes	42	50.0	31	64.6	

* χ^2.
DM2 = type-2 diabetes mellitus; HBP = high blood pressure; HDL-cholesterol = high-density lipoprotein-cholesterol; BMI = body mass index; WHR = waist-to-hip ratio; MS = metabolic syndrome.
Source: archive of the HGZ No. 35, IMSS.

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