The value of the metabolic syndrome and the anthropemetric measures in cholelithiasis

Kolelitiyaziste antropometrik ölçümler ve metabolik sendromun değeri

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Abstract

Introductıon: The purpose of this study is to establish the rate of metabolic syndrome and the value of the anthropemetric measures in etiology of the cholelitiasis.

Method: One hundred elective cholecystectomy inpatients and 50 outpatients with complaints other than cholelitiasis were included in the study. The height, weight, waist circumference, hip circumference, and blood pressures were measured. Serum glucose, insulin, HbA1c, uric acid, total cholesterol, triglyceride, HDL, and LDL cholesterol levels were determined. HOMA value was calculated to evaluate insulin resistance. The patients were assessed in terms of metabolic syndrome according to NCEP/ATP III criteria.

Results: The average number of the delivery was higher in the cholelitiasis cases than the control group (p=0.013). The high waist/hip ratio has been shown to have effects on cholelitiasis development in both sexes (p<0.05). The mean waist circumference was higher in the females with cholelitiasis as compared to women without cholelitiasis (p=0.0001). The risk of cholelitiasis was increased in the presence of diabetes mellitus, or hipertension, or hiperlipide mia (p=0.003). The average HOMA levels was found to be higher in the cholelitiasis cases significantly, and cholelitiasis risk was 1.92-fold higher in the patients with high HOMA levels. The risk of cholelitiasis was increased 2.43-fold higher in the patients with metabolic syndrome (p=0.015).

Özet

Amaç: Bu çalışmada safra kesesi taşı olan hastalarda metabolik sendrom rastlanma oranı ve antropometrik ölçümlerin etyolojideki yerinin belirlenmesi amaçlanmıştır.

Metot: Araştırmamıza elektif kolesistektomi için yatırılan 100 hasta ile safra kesesi taşı dışında bir nedenle polikliniğine başvuran 50 hasta dahil edildi. Hastaların boy, kilo, bel çevresi, kalça çevresi ölçümleri ve kan basıncı ölçümleri yapıldı. Serum glukoz, insülin, HbA1c, ürik asit, total kolesterol, trigliserit, HDL, LDL kolesterol seviyeleri değerlendirildi. İnsülin direncini belirlemek için HOMA değeri hesaplandı. Hastalar metabolik sendrom açısından NCEP / ATP III kriterlerine göre değerlendirildi.

Bulgular: Safra kesesi taşı olanlarda olmayanlara göre ortalama doğum sayısının daha yüksek olduğu belirlendi (p=0,013). Her iki cinste bel/kalça oranının yüksek olması safra kesesi taşı gelişiminde etkili olarak tespit edildi (p<0.05). Ortalama bel çevresi safra kesesi taşı olan kadınlarda safra kesesi taşı olmayanlara göre daha yüksek olarak tespit edildi (p=0,0001). Safra kesesi taşı olanlarda diabetes mellitus, hipertansiyon ya da hiperlipidemi durumunun varlığı kontrol gurubuna göre anlamlı olarak daha yüksek bulundu (p=0.003). Ortalama HOMA değeri kolelitiyazis gurubunda anlamlı olarak daha yüksek olup, yüksek HOMA değeri olan hastalarda safra kesesi taşı görülme riskinin 1.92 kat arttığı saptandı. Metabolik sendromu olanlarda da safra kesesi taşı riskinin 2.43 kat artmış olduğu tespit edildi (p=0.015).

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Conclusion: Cholelitiasis development was significantly associated with metabolic syndrome presence, high waist/hip ratio, antihypertensive and antidiabetic drug usage in both sexes, and high waist circumference and high delivery number in females.

Key words: Cholelitiasis, Metabolic syndrome, Obesity

Sonuç: Her iki cinsde kolelitiazis gelişme riskinin metabolik sendrom varlığı, yüksek bel/kalça oranı, antihipertansif ve antidiabetik ilaç kullanımı ile anlamlı olarak ilişkili olduğu, ayrıca kadınlarda yüksek bel çevresi ve doğum sayısı fazlalığının kolelitiyazisle ilişkili olduğu saptandı.

Anahtar Kelimeler: Kolelitiazis, Metabolik sendrom, Obezite

Introduction

The prevalence of cholelitiasis differs among countries according to several factors including genetic, lifestyle, and nutrition. The relationship between obesity and cholelithiasis is well known for years[1-3]. "Metabolic Syndrome" (MS) associated with obesity is a combination of abnormal metabolic conditions including insulin resistance, abdominal obesity, glucose intolerance or dyslipidemia, and hypertension[4-7]. Following the description of MS, a few studies were performed to examine its relationship with cholelitiasis. This study aimed to identify the role of MS which has serious effects on public health as an etiology of cholelitiasis.

Materials and methods

The study group consisted of 100 symptomatic cholelitiasis inpatients who were referred to S.B. Ankara Training and Research Hospital General Surgery Clinic for an surgical operation. The control group consisted of age-matched and sex-matched 50 outpatients without cholelitiasis. The exclusion criteria for participation in this study: The patients on antidepressant and antipsychotic treatment, the patients with polycystic over disease, sleep-apnea syndrome, the patients who had underwent surgical operations that may lead cholelitiasis such as truncal vagotomy, ileal resection, and bariatric surgery or the patients with hyperparathyroidism, hemolytic anemia, ileal diseases, artificial heart valves, and the patients who received total parenteral nutrition.

Height and weight were measured and BMI (kg/m^2) were calculated for all patients. Hip circumference, waist circumference and arterial tension, blood glucose, uric acid, HbA1c, insulin, LDL, HDL, triglyceride, and total cholesterol levels were recorded. Hepatobiliary sonography was performed to evaluate gallbladder in both groups. Homeostasis Model Assessment-Insulin Resistance test (HOMA-IR) was performed to evaluate insulin resistance (HOMA-IR= fasting insulin (mU/l) x fasting plasma glucose (mg/dl)) / 405). HOMA value was accepted as 2.7 according to Turkey Endocrinology and Metabolism Society Metabolic Syndrome Study Group 2009 Guideline for metabolic syndrome[8]. NCEP/ATP III criteria was used for MS diagnosis. Antidiabetic, antihypertensive, and antilipidemic drug usage was considered as positive criteria for MS parameters.

The statistical data evaluation was performed by SPSS (Statistical Program for Social Sciences version 11.5) package program. Khi-Square test and Fisher's Exact test were used for categorical data during intergroup comparisons, and Student's T test and Mann-Whitney U test were used for measuremental data. Odds ratio and 95% confidence interval were used to identify the factors which play a role during cholelitiasis.

Tablo 1. Evaluation of patiens accordig to the NCEP/ATP III criteria, (F: Female, M: Male)

	Cholelitiasis	Control	P
Abdominal Obesity (High WHR)	61/100 (61%)	17/50 (34%)	F: 0.039, M: 0.002
Hypertryglyceridemia	47/100 (47%)	16/50 (32%)	0.079
Low HDL	72/100 (72%)	29/50 (58%)	F: 0.113, M: 0.393
Hypertension	39/100 (39%)	10/50 (20%)	0.019
Hyperglysemia	30/100 (30%)	6/50 (12%)	0.015

Results

In the study group, there were 15 male (15%) and 85 female (85%) participants. The control group included 10 male (20%) and 40 female (80%) subjects. No statistically significant difference was found in terms of sexes between the two groups (p=0.05). The mean age was 52.8±15.01 in the study group and 54.6±16.02 in the control group, in which no statistically significant difference was found. Median parity was 4 (0-13) in the patients with cholelitiasis, and 3 (0-9) in the control group (p<0.013).

When the patients were assessed according to the BMI, no significant difference was found between groups (p>0.05). Similarly, waist circumferences were compared between groups, no difference was found for male patients. However, waist circumference was significantly higher in the female patients with cholelitiasis (p=0.0001, estimated relative risk [OR]=4.7). When waist-hip circumferences were compared between groups, waist/hip ratio (WHR) was significantly higher in the male and female cholelitiasis patients (Female: p=0.039, OR=2.13; Male: p=0.002, OR=2.5). ***(Table 1)***.

When the patients were compared based on MS presence according to NCEP/ATPIII criteria, the incidence of MS co-morbidity was found significantly higher in the cholelitiasis group, and the cholelitiasis risk was 2.43-fold higher in the MS patients ***(Table 1, Table 2)***.

When the patient groups were compared according to MS parameters, the incidence of diabetes (DM), hypertension (HT) or hyperlipemia (HL) associated with MS was found significantly higher in the cholelitiasis group (p=0.003). The prevalence of drug usage related these disorders was significantly higher in the cholelitiasis group (p=0.001). When the drug usage was evaluated separately, the prevalence of using antihypertensive and antidiabetic drugs was found higher in the cholelitiasis group (p=0.019, p=0.015); however, no difference was found in antilipidemic drug usage between the two groups.

In the cholelitiasis group the patients using antidiabetic drugs and the patients whose fasting blood glucose levels ≥110 mg/ml were higher as compared to control group (p=0.015, OR=3.14, 95% CI=1.21-8.16). During risk analyses, cholelitiasis risk was 3.14-fold higher in the patients with high blood glucose levels (OR=2.43, 95% Confidential interval [CI]=1.18-4.99). In addition, HbA1c levels were higher in the cholelitiasis patients as compared to the control group (6.21±1.2, 5.59±0.6; p<0.001).

A marked difference was found in average HOMA values between groups (4.75±4.6, 3.20±3.05; p= 0.016). The patients whose HOMA value was found above the 2.7 critical level were significantly higher in the cholelitiasis group (54%, 38%; p=0,065). The results revealed that the cholelitiasis risk increased 1.92- fold in the patients with high HOMA levels (OR=1.92, 95% CI=0.95-3.83), ***(Table 2)***. The mean insulin levels were significantly higher in the cholelitiasis group as compared to the control group (16.42±12.1, 12.42±7.2; p=0,034).

No significant difference was found in total cholesterol, LDL, triglyceride, and HDL values between groups. However, despite of drug usage, the cholelitiasis risk was 1.88-fold higher in the patients with high triglyceride levels, (OR=1.88, 95% CI=0.92-3.84). The cholelitiasis risk increased 1.88-fold in the female patients with low HDL levels, and 1.83-fold in the male patients with low HDL levels, (OR=1.88, 95% CI=0.33-10.09; OR=1.83, 95% CI=0.86-4.12). ***(Table 3)***.

Discussion

Cholelitiasis may be associated with several etiological factors including genetic, age, sex, obesity, diet, diabetes, hyperlipemia, small intestine pathologies, hemolytic anemia[9].

Tablo 2. HOMA values and MS incidence in the patients with and without cholelitiasis

	Cholelitiasis	Control	OR*	95% CI**	P
HOMA value (mean)	4.75 ± 4.6	3.20 ± 3.1			0.016
HOMA ≥2.7	54/100 (54%)	19/50 (38%)	1.92	0.95-3.83	0.065
Metabolic Syndrome presence (NCEP/ATPIII)	51/100 (51%)	15/50 (30%)	2.43	1.18-4.99	0.015

*Estimated relative risk
**Confidential interval

Tablo 3. Relationship between cholelitiasis and hiperlipidemia, and risk ratios (Patients using drugs were included)

	Cholelitiasis	Control	OR*	95% CI**	P
High total cholesterol level	46/100 (47%)	29/50 (58%)	**0.62**	**0.31-1.22**	**0.166**
High triglyceride level	47/100 (47%)	16/50 (32%)	1.88	0.92-3.84	0.079
High LDL level	17/100 (17%)	13/50 (26%)	0.58	0.26-1.32	0.194
HDL<50mg/dl (Female)	61/85 (71.8%)	23/40 (57.5%)	1.88	0.85-4.12	0.113
HDL<40mg/dl (Male)	11/15 (73.3%)	6/10 (60%)	1.83	0.33-10.09	0.393

*Estimated relative risk
**Confidential interval

In the cholelitiasis group, 15 patients were male (15%) and 85 were female (85%) subjects, predicating that the incidence was approximately 5.7-fold higher in the females. A study performed by Roma GREPCO showed that Female/Male ratio was 2-3:1 in Europe, and this difference decreased after 5th decade. A study performed by Sampliner showed that Female/Male ratio was 10:1 in 20-30 years old group[10,11]. In our study, mean parity was significantly higher in the patients with cholelitiasis, suggesting that pregnancy had an important etiologic role. Valdivieso reported that the incidence of bile mud was 30% and the incidence of cholelitiasis was 1-3% in the pregnant patients[12].

BMI is used to determine total body fat distribution, waist circumference or WHR is used to determine abdominal fat content[13]. Abdominal obesity is an important factor for cholelitiasis. The risk of cholelitiasis increases linearly with obesity degree in female patients; however, this effect is weak for male patients[10,14-20]. In our study, no significant difference in BMI was found in male and female patients between groups. According to the cholelitiasis risk studies, waist circumference is more predictive than BMI for male patients[20,21]. In our study the increase of waist circumference did not effect cholelitiasis risk in the male patients, but enhanced the cholelitiasis risk 4.7-fold in female patients ($p<0.0001$, OR=4.7). When high WHR values were assessed , the cholelitiasis risk increased 2.5-fold in male patients, and 2.1-fold in female patients, significantly.

The International Diabetes Federation (IDF) proposed a definition of the MS in 2005, which designated central obesity as mandatory[22]. The three most important risk factors for MS are obesity, body fat distribution disorder, and insulin resistance[13]. The study performed by Mendez-Sanchez N. et al. to establish an association between the MS and the cholelitiasis showed that MS was present in 40% of cholelitiasis subjects, compared with 17.2% of the controls, and the presence of three criteria of MS conferred a 7.89-fold increased risk of having cholelitiasis[14]. In our study, MS was present in 51% of cholelitiasis subjects as compared to 30% of the controls, and MS conferred a 2.43-fold increased risk of having cholelitiasis.

Previous research studies show that diabetes is a risk factor for cholelitiasis. In a research study, Shreiner et al. indicated that DM might delay emptying of the gallbladder; therefore, it might predispose cholelitiasis[23]. De Santis et al. showed that DM was a risk factor for cholelitiasis, and this effect was more pronounced in female patients as compared to male patients[19]. In the cholelitiasis group the patients using antidiabetic drugs and the patients whose fasting blood glucose levels ≥110 mg/ml were higher as compared to control group. In addition, cholelitiasis risk was 3.14-fold higher in the patients with high blood glucose levels . Insulin resistance in tissues precedes the development of type 2 diabetes[24]. In addition, insulin resistance has a major role for MS[5]. In our HOMA index study on insulin resistance, the rate of cases with high HOMA index was higher in cholelitiasis group as compared to control group, however, no significant difference was found (54%, 38%; $p=0.065$). But this number is come near to the level of the significance. The cholelitiasis risk increased 1.92-fold in the patients with high HOMA levels, and the mean HOMA values were found higher in the cholelitiasis group as compared to the control group, significantly. The previous studies have supported our results. In the experimental study performed by Biddenger, insulin resistance increased the cholelitiasis risk[25]. In the other study performed by Ko., insulin resistance identified by HOMA values was distinctly higher in the female patients with cholelitiasis or bile mud, and increased insulin level was a risk factor for the cholelitiasis[26].

Lonescu reported that arterial hypertension coexisted with cholelitiasis significantly[27]. Mendez-Sanchez stated that blood pressure, especially systolic blood pres-

sure was associated with MS and cholelitiasis[14]. Similarly in our study, the incidence of antihypertensive drug usage was higher in patients with cholelitiasis than the control patients, significantly.

In this study, no significant difference was identified in antihyperlipemic drug usage between groups. No significant difference was found in total cholesterol and triglyceride values between groups. However, the cholelitiasis risk was 1.88-fold higher in the patients with high triglyceride levels. No significant difference in LDL and HDL levels was found between groups (p>0,05), but the cholelitiasis risk increased 1.88-fold in the female patients with low HDL levels, and 1.83-fold in the male patients with low HDL levels. Even though we could not show apparently, hyperlipidemia is an important risk factor for cholelitiasis. Reseach studies show that especially low HDL levels and high triglyceride levels increase the cholelitiasis risk[5,28,29].

According to the study results, cholelitiasis development was associated with metabolic syndrome presence, high waist/hip ratio, antihypertensive and antidiabetic drug usage in both sexes, and high waist circumference and delivery number in females.

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