Cholelithiasis may also be a consequence of metabolic syndrome

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Abstract

Background: We tried to understand whether or not there is a significant relationship between cholelithiasis and parameters of the metabolic syndrome.

Methods: The study was performed in Internal Medicine Polyclinics on routine check up patients. All cases with cholelithiasis or already performed cholecystectomy for cholelithiasis were put into the first group and age and sex-matched control cases were put into the second group.

Results: One hundred and fourty-four cases either with cholelithiasis or already performed cholecystectomy for cholelithiasis were detected among 3.437 cases, totally (4.1%). One hundred and sixteen (80.1%) of them were female with a mean age of 53.6 years. Obesity was significantly higher (54.8% versus 43.7%, p<0.01) and normal weight was significantly lower (7.6% versus 18.0%, p<0.01) in the cholelithiasis group, and the mean body mass indexes (BMI) were 31.0 versus 28.9 kg/m2 in them, respectively (p<0.01). Probably parallel to the higher mean BMI, prevalences of hypertension (26.3% versus 13.1%, p<0.001) and hypertriglyceridemia (25.0% versus 18.0%, p<0.05) were also higher in the cholelithiasis group, significantly. On the other hand, hyperbetalipoproteinemia was significantly lower in the cholelithiasis group with unknown reasons (9.7% versus 18.0%, p<0.05).

Conclusions: Cholelithiasis is a common pathology in society and nearly four-fold more frequent in women, particularly in their fifties. There are significant relationships between cholelithiasis and parameters of the metabolic syndrome including female predominance, elder age, BMI, obesity, hypertension, and hypertriglyceridemia. On the other hand, the significantly lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients should be researched with further studies.

Key words: Cholelithiasis, metabolic syndrome, obesity, hyperbetalipoproteinemia

Introduction

Chronic endothelial damage may be the most common type of vasculitis and the leading cause of aging, morbidity, and mortality in human beings. Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on endothelium, and probably whole afferent vasculature including capillaries, are involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic natures that reduce blood flow and increase systolic BP further. Some of the well-known indicators of the inflammatory process are sedentary life style, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose, impaired glucose tolerance, white coat hypertension, and other chronic inflammatory processes including rheumatologic disorders, prolonged infections, and cancers for the development of irreversible consequences including obesity, hypertension, diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary artery disease (CAD), mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and death. Although early withdrawal of causative factors may prevent final consequences, after development of cirrhosis, COPD, CRD, CAD, PAD, or stroke, endothelial changes cannot be reversed completely due to their fibrotic natures. They were researched under the title of metabolic syndrome in the literature, extensively (1-4). On the other hand, gallstone is also found among one of the most common health problems in developed countries (5), and it is particularly frequent in women above the age of 40 years (6). Most of the gallstones are found in the gallbladder, which is also called cholelithiasis. Its pathogenesis is uncertain and it appears to be influenced by genetic and environmental factors (7). Excess weight is a known and age-independent risk factor for gallstone (8). Delayed bladder emptying, decreased small intestinal motility, and sensitivity to cholecystokinin were associated with obesity and gallstone disease (9). An increased risk was confirmed in obese diabetics with hypertriglyceridemia (10), and plasma cholesterol levels were found related with gallstone (11). Even more conflicting results were reported about an association between gallstone and smoking (12-14). We tried to understand whether or not there is a significant relationship between cholelithiasis and parameters of the metabolic syndrome.

Materials and Methods

The study was performed in Internal Medicine Polyclinics of the Dumlupinar and Mustafa Kemal Universities on routine check up of patients between August 2005 and November 2007. We took consecutive patients below the age of 70 years to avoid debility induced weight loss in elders. Their medical histories, including smoking habit, hypertension, DM, dyslipidemia, and already used medications and performed operations were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an abdominal ultrasonography was performed. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Current daily smokers for the last six months and cases with a history of five pack-years were accepted as smokers. Cigar or pipe smokers were excluded. Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions since there is evidence that heavier individuals systematically underreport their weight (15). Weight in kilograms is divided by height in meters squared, and underweight is defined as a BMI of lower than 18.5, normal weight as 18.5-24.9, overweight as 25.0-29.9, and obesity as a BMI of 30.0 kg/m2 or greater (16). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already receiving antidiabetic medications were defined as diabetics (16). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 125 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level 200 mg/dL or greater is DM (16). Patients with dyslipidemia were detected, and we used the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups (16). Dyslipidemia is diagnosed when LDL-C is 160 or higher and/or TG is 200 or higher and/or HDL-C is lower than 40 mg/dL. Office BP was checked after a 5-minute rest in seated position, with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after a 10-minute education session about proper BP measurement techniques (17). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurement. An additional 24-hour ambulatory BP monitoring was not required due to the equal efficacy of the method with HBP measurement to diagnose hypertension (18). Eventually, hypertension is defined as a BP of 135/85 mmHg or greater on HBP measurements (17). Cholelithiasis was diagnosed ultrasonographically. Eventually, all cases either with presenting cholelithiasis or already performed cholecystectomy for cholelithiasis were put into the first group and age and sex-matched control cases were put into the second groups. Prevalences of smoking, normal weight, overweight, obesity, hypertension, DM, hypertriglyceridemia, hyperbetalipoproteinemia, and dyslipidemia and mean BMI values were detected in both groups and compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

Although the exclusion criteria, 119 cases with cholecystectomy for cholelithiasis and 25 with already presenting asymptomatic cholelithiasis were detected among 3.437 cases, total (4.1%). One hundred and sixteen (80.1%) of them were female with a mean age of 53.6 years, so cholelithiasis is mainly a disorder of females in their fifties. Prevalences of smoking were similar in the cholelithiasis and control groups (18.0% versus 19.4%, p>0.05, respectively). There was not any patient with underweight. Interestingly, 92.3% (133 cases) of the cholelithiasis group had excess weight and only 7.6% (11 cases) of them had normal weight. Obesity was significantly higher (54.8% versus 43.7%, p<0.01) and normal weight was significantly lower (7.6% versus 18.0%, p<0.01) in the cholelithiasis group. Mean BMI values were 31.0 and 28.9 kg/m2, (p<0.01) in them. Probably parallel to the higher mean BMI, prevalences of hypertension (26.3% versus 13.1%, p<0.001) and hypertriglyceridemia (25.0% versus 18.0%, p<0.05) were also higher in the cholelithiasis group, significantly. Differences were nonsignificant according to the prevalences of DM and dyslipidemia. On the other hand, hyperbetalipoproteinemia was significantly lower in the cholelithiasis group with unknown reasons (9.7% versus 18.0%, p<0.05) (Table 1).

Table 1: Comparison of cases with and without cholelithiasis

Variable	Cases with cholelithiasis or cholecystectomy for cholelithiasis	Control cases	*p*-value
Number	144	144	
Female ratio	80.5% (116)	80.5% (116)	
Mean age (year)	53.6 ± 9.3 (27-70)	53.6 ± 10.2 (28-70)	Ns*
Prevalence of smoking	18.0% (26)	19.4% (28)	Ns
Mean BMI† (kg/m2)	***31.0 ± 6.1 (19-51)***	***28.9 ± 5.7 (19-52)***	***<0.01***
Prevalence of normal weight	***7.6% (11)***	***18.0% (26)***	***<0.01***
Prevalence of overweight	37.5% (54)	38.1% (55)	Ns
Prevalence of obesity	***54.8% (79)***	***43.7% (63)***	***<0.01***
Prevalence of hypertension	***26.3% (38)***	***13.1% (19)***	***<0.001***
Prevalence of DM‡	20.8% (30)	19.4% (28)	Ns
Prevalence of hyperbetalipoproteinemia	***9.7% (14)***	***18.0% (26)***	***<0.05***
Prevalence of hypertriglyceridemia	***25.0% (36)***	***18.0% (26)***	***<0.05***
Prevalence of dyslipidemia	31.9% (46)	29.8% (43)	Ns

*Nonsignificant (p>0.05)
†Body mass index
‡Diabetes mellitus

Discussion

Excess weight leads to both structural and functional abnormalities of many organ systems of the body. Recent studies revealed that adipose tissue produces biologically active leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin which are closely related with the development of complications (19). For instance, the cardiovascular field has recently shown a great interest in the role of inflammation in development of atherosclerosis and numerous studies indicated that inflammation plays a significant role in the pathogenesis of atherosclerosis and thrombosis (20, 21). Adipose tissue is involved in the regulation of cytokines (22). On the other hand, individuals with excess weight will have an increased circulating blood volume as well as an increased cardiac output, thought to be the result of increased oxygen demand of the excessive fat tissue. The prolonged increase in circulating blood volume can lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of hypertension. In addition to the hypertension, the prevalences of high FPG, high serum total cholesterol, and low HDL-C, and their clustering were all raised with the higher BMI (23). Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke with higher risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the incidences of CHD and stroke have increased with a higher BMI in the other studies (23, 24), and risk of death from all causes including cancers increases throughout the range of moderate and severe excess weight for both genders in all age groups (25). As another consequence of excess weight on health, the cholelithiasis cases had a significantly higher mean BMI in the present study (31.0 versus 28.9 kg/m2, $p<0.01$) similar to the previous reports (8, 9). Probably as a consequence of the significantly higher BMI, the prevalences of hypertension (26.3% versus 13.1%, $p<0.001$) and hypertriglyceridemia (25.0% versus 18.0%, $p<0.05$) were also higher in the cholelithiasis patients. The relationship between excess weight and elevated BP and hypertriglyceridemia is already described in the metabolic syndrome (26), and clinical manifestations of the syndrome include obesity, dyslipidemia, hypertension, insulin resistance, and proinflammatory as well as prothrombotic states (27). The above confirmed increased risk of cholelithiasis in obese diabetics with hypertriglyceridemia may also be an indicator of its association with the metabolic syndrome (10, 26). Although the presence of some conflicting results in the literature (12-14), we did not find any significant association between cholelithiasis and smoking in the present study ($p>0.05$). On the other hand, the lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients in the present study (9.7% versus 18.0%, $p<0.05$), although the significantly higher mean BMI values of them, should be researched with further studies. As a conclusion, cholelithiasis is a common pathology in society and nearly four-fold more frequent in women, particularly in their fifties. There are significant relationships between cholelithiasis and parameters of the metabolic syndrome including female predominance, elder age, BMI, obesity, hypertension, and hypertriglyceridemia. On the other hand, the significantly lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients should be researched with further studies.

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