# Body weight gain as the major risk factor of cholelithiasis in women and an important risk factor in man

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### Abstract

**Purpose:** The power of correlation was assessed between chosen risk factors of cholelithiasis in order to establish the ranking of these factors in Podlasie inhabitants.

Material and methods: The study involved 169 patients hospitalized due to cholelithiasis (study group) and 202 patients without cholelithiasis (control group). Previous exposure of patients of both groups to the chosen risk factors of cholelithiasis was evaluated (based on a history questionnaire designed by the authors of the study). Two models of logistic regression were prepared (for men and women) for multivariate analysis.

**Results:** The ranking of the risk factors of cholelithiasis was established by analysing multiple correlation coefficients for the two models of logistic regression and their significance was determined with Wald's test. The significant risk factors for women included: overweight and obesity, age, diabetes, use of contraceptive pills, while for men these were: age, serum triglycerol level, obesity.

Conclusions: The knowledge of risk factors of cholelithiasis in our population is the essence of health promoting actions. Obesity is the major risk factor in women and statistically significant in men. Promotion of appropriate eating habits can result in body mass reduction and may thus indirectly decrease other risk factors of cholelithiasis (incidence of type II diabetes and serum triglycerol level).

Key words: cholelithiasis, obesity, risk factors, adults.

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### Introduction

Cholelithiasis belongs to the most common diseases of the digestive system and its incidence is growing steadily. It is assumed that in Poland over 11.0% of the whole population suffer from this ailment [1]. However, there is a lack of population surveys and therefore epidemiological data seem to be incomplete. Studies performed in work institutions have contributed to the determination of the cross-sectional prevalence of the disease in the occupationally active group (aged 18-70 years) of inhabitants in the south of Poland. Cholelithiasis was found there in approximately 12.0% of patients (17.36% women and 6.41% men) [2]. In Szczecin, cholelithiasis was diagnosed in 17.33% of women working in industrial plants (aged 20-69) [3], the percentage of women with concretions in the gallbladder being 1.66% for the age of 20-29 and 35.29% for 60-69 years.

Studies on cholelithiasis tend to identify risk factors, being of great value for effective prevention. It is assumed that gallstone formation is associated with a combination of genetic and environmental factors, i.e. female gender, positive family history, hyperlipidaemia, obesity, age, number of labours and abortions, type I and II diabetes, diseases of the colon, use of hormonal contraceptives, some of the gastrointestinal tract disorders (e.g. malabsorption syndrome, polycystic fibrosis of the pancreas with excretory failure, diseases impairing functioning of the gallbladder and others) [4-8]. The aim of the present study was to determine mutual correlations of chosen risk factors of cholelithiasis in the population of patients from Podlasie and in consequence to establish more effective measures of the disease prevention and health promoting attitudes.

#### Material and methods

Risk factors of cholelithiasis were retrospectively assessed using a history questionnaire form (designed by the authors of the study). The study involved 169 patients hospitalized in III Department of Internal Diseases and Gastroenterology of

Table 1. Model I of logistic regression for women n=227

Variables	Regression coefficient	Wald's test
1. Age	0.0475	<u>0.0001</u>
2. Body mass index (BMI)	0.1592	<u>0.0000</u>
3. Education	0.0532	0.8468
4. Type of leisure	-0.7385	0.0899
5. Diabetes	1.1963	<u>0.0343</u>
6. Cholelithiasis positive family history	0.0032	0.9944
7. Diabetes positive family history	0.9386	0.0380
8. Use of contraceptive pills	-1.8693	<u>0.0123</u>
9. Number of labours and abortions	-0.2946	0.0760
10. Use of cholesterol-reduction drugs	0.5227	0.5069
11. Level of serum triglycerols (TG)	0.5581	0.0854
12. Total cholesterol	0.2074	0.5359
13. HDL-cholesterol	0.2708	0.4328
Constant	-7.0165	0.0140

Table 2. Model II of logistic regression for men n=144

Variables	Regression coefficient	Wald's test
1. Age	0.0477	0.0014
2. Body mass index (BMI)	0.0980	0.0276
3. Education	-0.2468	0.3818
4. Type of leisure	-0.7355	0.0955
5. Diabetes	0.3430	0.5821
6. Cholelithiasis positive family history	0.2142	0.6922
7. Diabetes positive family history	0.9404	0.1489
8. Use of cholesterol-reduction drugs	-0.2944	0.6843
9. Level of serum triglycerols (TG)	1.1598	0.0048
10. Total cholesterol	-0.0347	0.9340
11. HDL-cholesterol	-0.0081	0.9861
Constant	-6.5978	0.0152

The District General Hospital in Białystok, with cholelithiasis diagnosed based on clinical observations, ultrasound of the abdominal cavity and/or endoscopic retrograde pancreatocholangiography (group I). Control group included 202 cholelithiasis-free patients treated in the same department, who were selected by stratified randomisation method. Efforts were taken to match the patients of both groups for age, gender and the place of living.

Multivariate logistic regression analysis was employed to identify the factors that significantly increase the risk of cholelithiasis. Two separate models of logistic regression were designed to assess the risk factors according to gender (model I – 13 factors, for women and model II – 11 factors, for men). Model I contained the following risk factors: age, body mass index (BMI), education, type of leisure, diabetes, cholelithiasis and/or diabetes positive family history, use of contraceptive pills, number of labours and abortions, use of cholesterol-reducing drugs, level of serum triglycerols (TG), total cholesterol and HDL-cholesterol. Model II consisted of the same risk factors except for hormonal contraception and number of labours and abortions. The models were assessed statistically using SPSS package for Windows Release 6.0. Significance of the respective factors was tested with bilateral Wald's test, with p values < 0.05 considered to be significant. Then, based on the 2x2 table (four-field) sensitivity, specificity and predicted accuracy of the method were determined. The category of predicted cholelithiasis was identified when the calculated probability equalled 0.5 (pg=0.5). The calculated power of correlation between logistic regression coefficients of the respective risk factors was used to establish their ranking.

#### Results

The study involved 169 cholelithiasis patients (109 women and 60 men) aged 23-91 years (mean - 63.8 years) and 202 cholelithiasis-free patients (118 women and 84 men) aged 19-90 years (mean - 55.6 years). The majority of patients (75.2%

women and 81.7% of men) lived in town, the remaining patients inhabited the adjacent villages.

Model I of logistic regression, presented in *Tab. 1*, was designed to determine mutual correlations between the investigated risk factors of cholelithiasis in women. 227 women were recruited (109 with and 118 without cholelithiasis) and 13 risk factors were investigated. Such parameters as overweight and obesity, age, diabetes (family history of diabetes was on the border of significance p=0.0621) and the use of hormonal contraceptives appeared to be the significant prognostic factors of cholelithiasis in women. The method sensitivity, specificity and predicted accuracy were calculated for 5 of the risk factors, being 71.6%, 71.2% and 71.4%, respectively.

A similar model of logistic regression was designed for 144 men (60 with cholelithiasis and 84 without). Eleven risk factors were assessed (excluding 2 typical for women i.e. contraception and labours). The results are presented in *Tab. 2*. The significant prognostic factors in men were (depending on the correlation power): age, current serum TG level and high BMI. The method sensitivity, specificity and predicted accuracy were calculated for these three factors, being 58.3%, 78.6% and 70.1%, respectively.

The analysis of multiple correlation coefficients of the two logistic regression models and Wald's test revealed the following order of risk factors:

• Women – statistically significant factors: 1. overweight and obesity, 2. age, 3. diabetes, 4. use of contraceptive pills – close to statistical significance, 5. positive family history of diabetes, 6. number of labours and abortions, 7. serum TG, 8. type of leisure; and statistically insignificant factors, 9. serum HDL-cholesterol, 10. use of cholesterol-reducing drugs, 11. serum total cholesterol, 12. education, 13. positive family history of cholelithiasis.

• Men – statististically significant factors: 1. age, 2. serum TG, 3. obesity, close to statistical significance: 4. type of leisure; and statistically insignificant factors: positive family history of diabetes, 6. education, 7. diabetes, 8. use of cholesterol-reducing drugs, 9. positive family history of cholelithiasis, 10. serum total cholesterol, 11. serum HDL-cholesterol.

## Discussion

Cholelithiasis has been long known to be a multifactorial disease and to have higher incidence among women. Many authors have assessed correlations of risk factors of cholelithiasis using multifactorial analysis with logistic regression based on models designed for males and females [9,10]. In one of such studies, age, gender, active hepatitis, obesity, hyperlipidemia and diabetes were analysed [11]. Age and diabetes turned out to be statistically significant risk factors of cholelithiasis in both genders. In another study, carried out on patients aged 20-74 [12], the significant factors included: in men - age, education, subscapular fold thickness, high HDL-cholesterol level; in women - age, BMI, skin fold thickness, diabetes, glucose tolerance disorders and oral contraceptives. Alcohol intake had no significant effect on the incidence of cholelithiasis in both genders. Similar findings were obtained in the present study. High BMI, concomitant diabetes, use of contraceptive pills and positive family history of diabetes were the prognostic factors of cholelithiasis (predicted accuracy 71.4%). In an American study performed on 425 women under 45 years of age [9] the logistic regression model included: the use of oral contraceptives, BMI, changes in body weight, alcohol consumption, past pregnancies, smoking. The elevated BMI, especially in young women and in those after at least 4 labours was a statistically significant factor predisposing to cholelithiasis. Unlike in our study, low correlation power was observed between the use of oral contraceptives and cholelithiasis, which was slightly higher when contraceptives had been taken for over 15 years. The correlation power was increasing slightly in currently smoking women, as compared to non-smokers. However, the analysis of logistic regression of risk factors of cholelithiasis in men in Japan has revealed that alcohol consumption reduces the risk of cholelithiasis, BMI - positively correlates with cholelithiasis, glucose intolerance only slightly increases the risk and diabetes is not a risk factor [10]. In our study, concomitant diabetes was not a risk factor of cholelithiasis in men, but the risk occurred with obesity and high serum triglycerol level.

Thus, both the outcome of our study and the findings obtained by other authors seem to indicate that cholelithiasis etiology depends largely on the power of synergistic action of the respective risk factors. In women from Podlasie these factors include: overweight or obesity, age, diabetes and the use of contraceptive pills; to a lesser extent positive family history of diabetes, number of labours and abortions, serum TG levels and passive leisure. In men from Podlasie, these are: age, elevated TG levels, obesity and to a lesser degree passive leisure. The presented hereby ranking of factors predisposing to cholelithiasis in both genders indicates health related needs and points at high risk groups. The essence of promoting actions is a change of bionegative behaviours and favouring healthy lifestyle. In many countries, health promotion is regarded as the only alternative for the steadily increasing health protection expenses [13]. Age and gender are the risk factors of cholelithiasis independent of health promoting actions. However, a lot can be done to reduce overweight and obesity, as well as indirectly diminish the incidence of insulin-dependent diabetes or serum TG level. The beneficial effect of physical activity should be constantly emphasized. The preventive measures can be divided into several stages [14,15]. In the first stage, patients with elevated BMI and serum glucose and/lipid levels (especially TG) are detected and subjected to intensive preventive treatment. In the second stage, efforts are made to reduce the above parameters in the whole population by promoting proper nutrition and physical activity [16].

Concluding, the presented hereby ranking of the risk factors of cholelithiasis in women and men allows determination of groups being at high risk of this disease. Health promoting behaviours in these subjects should tend towards body mass normalization, promotion of healthy diet, and active leisure.

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