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Non-alcoholic fatty liver disease in women with polycystic ovary syndrome — clinical and metabolic aspects and lipoprotein lipase gene polymorphism

Niealkoholowe stłuszczenie wątroby u kobiet z zespołem wielotorbielowatych jajników — aspekty kliniczne i metaboliczne oraz polimorfizm genu lipazy lipoproteinowej

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Abstract

Introduction: The aim was to assess associations among PCOS and NAFLD, the lipoprotein lipase polymorphism gene, and metabolic disorders in PCOS.

Material and methods: In 184 women with PCOS and 125 healthy, premenopausal volunteers, sex steroids, lipids, glucose, insulin, aminotransferases, free androgen index (FAI), HOMA-IR and E2/T were calculated. Hepatic steatosis was determined by ultrasound. Whole genomic DNA was isolated from blood leucocytes. Lipoprotein lipase polymorphisms rs268 and rs328 were analysed by polymerase chain reaction (PCR) and minisequencing.

Results: 57.6% of PCOS women had NAFLD, while women without PCOS had NAFLD in 49.6%. PCOS-NAFLD women had higher BMI, WHR and waist circumference compared to women with PCOS without NAFLD and women without PCOS. PCOS-NAFLD women had lower SHBG, E2/T ratio, and higher FAI compared to other groups. ALT levels were higher in PCOS women with NAFLD compared to other groups. PCOS women with and without NAFLD had higher fasting glucose and insulin and HOMA compared to women without PCOS. Women with PCOS had higher triglycerides and lower HDL-C compared to women without PCOS. There was no evidence that evaluated polymorphisms influenced hepatic steatosis in women with and without PCOS.

Conclusions: PCOS is not an independent factor influencing NAFLD in women. The influences on NAFLD incidence in women are BMI > 25 kg/m^2, glucose level > 80 mg/dL, E2/T < 80 and ALT > 19 IU/L as independent factors. Hyperandrogenism in PCOS may increase the risk of NAFLD indirectly by obesity, insulin resistance, and directly by the hepatotoxic effect. Polymorphisms rs328 and rs268 of the lipoprotein lipase gene do not affect the occurrence of NAFLD in women with PCOS or without PCOS. **(Endokrynol Pol 2014; 65 (6): 416–421)**

Key words: *nonalcoholic fatty liver disease; PCOS; lipoprotein lipase gene polymorphism*

Streszczenie

Wstęp: Celem pracy było zbadanie zależności między zespołem wielotorbielowatych jajników (PCOS) a niealkokoholowym stłuszczniem wątroby (NAFLD), polimorfizmem genu lipazy lipoproteinowej oraz zaburzeniami metabolicznymi obserwowanymi w PCOS.

Materiał i metody: W grupie 184 kobiet z PCOS i wśród 125 zdrowych kobiet premenopauzalnych badano w surowicy stężenia hormonów płciowych, frakcji lipidowych, glukozy insuliny i transaminaz oraz obliczano wskaźniki wolnych androgenów (FAI), insulinooporności HOMA i E2/T. Stłuszczenie wątroby oceniano ultrasonograficznie. Genomowe DNA izolowano z leukocytów krwi obwodowej metodami standardowymi. Do oznaczanie polimorfizmów rs268 i rs 328 lipazy lipoproteinowej użyto metody PCR i minisekwencjonowania.

Wyniki: częstość występowania NAFLD u kobiet z PCOS nie różniła się istotnie w porównaniu do kobiet bez PCOS. Kobiety z PCOS i NAFLD miały istotnie wyższy BMI , WHR i obwód talii w porównaniu z kobietami z PCOS bez NAFLD oraz kobiet bez PCOS. Ponadto stwierdzono u nich istotnie niższe SHBG, E2/T i wyższy FAI w porównaniu z kobietami z pozostałych grup. Stężenia transaminazy alaninowej (ALT) w grupie PCOS z NAFLD były istotnie wyższe niż w pozostałych grupach. U kobiet z PCOS z i bez NAFLD obserwowano istotnie wyższe stężenia glukozy, insuliny i wskaźnika HOMA w porównaniu z kobietami bez PCOS. Nie stwierdzono istotnych różnic w występowaniu określonych polimorfizmów genu lipazy lipoproteinowej w badanych grupach.

Wnioski: Zespół wielotorbielowatych jajników nie jest niezależnym czynnikiem wpływającym na NAFLD u kobiet. Niezależnymi czynnikami mającymi wpływ na wystąpienie NAFLD są: BMI > 25 kg/m^2, stężenie glukozy > 80 mg/dl, E2/T < 80 oraz ALT > 19 IU/l. Hiperandrogenizm w PCOS może pośrednio zwiększać ryzyko NAFLD przez insulinooporność i otyłość oraz bezpośrednio przez efekt hepatotoksyczny. Polimorfizmy rs320 i rs268 genu lipazy lipoproteinowej nie mają wpływu na częstość występowania NAFLD u kobiet z PCOS. **(Endokrynol Pol 2014; 65 (6): 416–421)**

Słowa kluczowe: *niealkoholowe stłuszczenie wątroby; zespół wielotorbielowatych jajników; polimorfizm genu lipazy lipoproteinowej*

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age, and affects 5–10% of this population [1–3]. Hyperandrogenism/hirsutism, oligo- or amenorrhea, and polycystic ovaries are the features of this syndrome, and at least two of the three symptoms listed above are required to recognise PCOS [4, 5]. About 50% of PCOS women are overweight or obese, with body fat mostly centrally located. Insulin resistance, dyslipidemia, risk for developing type 2 diabetes and hypertension with a subsequent risk of cardiovascular disease are very frequent, even in lean PCOS women [1–3]. Nonalcoholic fatty liver disease (NAFLD) is one of the most important hepatic manifestations of metabolic disturbances with a spectrum from hepatic steatosis, inflammation, fibrosis to hepatocellular carcinoma [6, 7]. Women with PCOS were recently reported to have a higher prevalence of NAFLD than women without this syndrome. The reasons were primarily considered to be related to the higher prevalence of obesity, dyslipidemia and insulin resistance in this population of women [8, 9]. However, it has been reported that PCOS itself still accounts for the higher risk of NAFLD and abnormal aminotransferase activity after consideration of the confounding effect of obesity [10]. The occurrence of NAFLD may also be influenced by lipoprotein lipase (LPL) activity, related inter alia to its genetic polymorphism. Several described LPL gene polymorphisms are associated with a higher incidence of insulin resistance and cardiovascular risk factors, but others could exert protective effects [11–14].

The aim of this study was to determine whether there is an association between PCOS and NAFLD, and whether in women with PCOS LPL gene polymorphism is associated with the aetiology of metabolic disorders occurring in these women.

Material and methods

184 obese and overweight (BMI > 25 kg/m^2) women (mean age 25.3 ± 6) affected by PCOS were enrolled in our study. The study protocol was approved by the Ethics Committee for Human Studies of Wroclaw Medical University. Informed written consent was obtained from all subjects after explanation of the nature, purpose and potential risks of the study.

PCOS was defined according to the Rotterdam criteria [4], when at least two of the following features were present after exclusion of other aetiologies: oligo- or anovulation (fewer than six menstrual periods in the preceding year), clinical (Ferriman-Gallwey score > 8) and/or biochemical signs of hyperandrogenism and polycystic ovaries. Ultrasound criteria used for diagnosis of PCO are the following: presence of 12 or more follicles in each ovary measuring 2–9 mm in diameter and/or increased ovarian volume (> 10 mL). Oligo- or amenorrhea was present in all PCOS women. All women had normal hepatic and renal functions. Their prolactin levels were within normal ranges and thyroid function was normal. An overnight dexamethasone suppression test (1 mg) and follicular phase serum 17-hydroxyprogesterone determination were performed to exclude Cushing's syndrome and the late-onset form of congenital adrenal hyperplasia.

The control group consisted of 125 healthy, premenopausal volunteers (mean age 27.7 ± 7) with regular menses and ultrasonographically normal ovaries.

Exclusion criteria for the study group and controls were: pregnancy, current or previous (within six months) use of oral contraceptives, anti-androgens or other hormonal drugs, known cardiovascular disease (CVD), diabetes mellitus, hypertension, cigarette smoking, history of liver diseases, and chronic alcohol consumption.

Protocol of the study

We calculated waist-to-hip ratio (WHR) as the quotient of waist and hip circumferences and body mass index (BMI) as body weight (kg) divided by square of body height (m). All subjects underwent abdominal and transvaginal ultrasonography. Ultrasound examination of liver steatosis was performed by a single examiner using a Toshiba APLIO 500 equipped with a 2–5 MHz convex array probe and 7–13 MHz linear array probe. Scans were performed after a fasting period of at least 6 h. According to established diagnostic criteria [15], the degree of fatty infiltration of the liver was classified as mild (hepatic steatosis grade 1), moderate (hepatic steatosis grade 2), or severe (hepatic steatosis grade 3). Biochemical parameters were measured in all women in the morning subsequent to an overnight fast, in control and study groups. Plasma was removed and stored at –20°C until analysed. Plasma total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C), glucose (G), lutropin (LH), follicle-stimulating hormone (FSH), total testosterone (T), sex hormone binding globulin (SHBG), C-reactive protein (CRP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were examined in all PCOS patients and the control group of women. In all women, peripheral insulin sensitivity was estimated using fasting insulin levels and homeostasis model assessment (HOMA) with the following validated formula: HOMA = $[(I_0) \times (G_0)/405]$ where I_0 it is fasting insulin (IN μU/mL) and G_0 is fasting glucose (in mg/dL). Index of free androgens (FAI) was calculated as: [total

Table I. *Primers' sequences used to LPL gene amplification*
Tabela I. *Sekwencja starterów wykorzystanych do amplifikacji fragmentów genu LPL*

Polymorphism	Forward PCR primer (5′-3′)	Reverse PCR primer (5′-3′)	Fragment size [bp]
rs268	ACG AGC GCT CCA TTC ATC TC	CAG TCT CCA GCC TAC CTT TG	230
rs328	TGG CCT GAG TGT GAC AGT TA	GAG GAA TGC ATG AAG CTG CC	330

testosterone ×100]/SHBG. Blood glucose was measured by the colorimetric method with the Dimension laboratory system (Dade Behring Ltd., England). Total cholesterol, HDL-C and triglycerides were measured by commercial enzymatic methods (BioMerieux, France). LDL-C was calculated using Friedewald's formula. Plasma LH, FSH, E2, T, SHBG, and insulin levels were measured by chemiluminescent enzyme immunoassays (Immulite 2000, DPC, USA). CRP was measured with a high sensitive immunonephelometry method using CardioPhase hsCRP reagent with the BN laboratory system (Dade Behring Marburg GmbH, Germany).

Whole genomic DNA was isolated from blood leucocytes using Blood Mini Kit produced by Macherey Nagel. *LPL* genotyping was performed by polymerase chain reaction (PCR) and minisequencing (Table I).

In order to amplify fragments of the LPL gene, we used a mix containing: 1x PCR buffer, 1.5 mM $MgCl_2$, 200 M dATP, 200 M dCTP, 200 M dGTP, 200 M dTTP, 1x Q solution, 2x polymerase units (TaKaRa), 200 ng genomic DNA, water up to 20 l and primers:

The DNA was denatured at 95°C for three minutes followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 55°C for 30 seconds, and extension at 72°C for 60 seconds. Amplified fragments were purified from oligonucleotides and free dNTPs by SAP and ExoI treatment (Fermentas).

The minisequencing method was based on the incorporation of single fluorescence-labelled dideoxynucleotides to the 3′ end of oligonucleotide which was correctly paired to the specific template DNA fragment using a SNaPshot kit (Applied Biosystems). The SNaPshot reaction was carried out using oligonucleotides:

— **rs268**: TTTTTTTTTCAATCTGGGCTATGAGATCA
— **rs328:** TTTTTTTTTTTTTTTTTTCAAGTCTCTGAATAAGAAGT
— designed so that it ended immediately before the polymorphic sides. The SNaPshot reaction consisted of 25 cycles: denaturation at 96°C for ten seconds, annealing at 50°C for five seconds, and extension at 60°C for 30 seconds.

Products were analysed by an ABI 3100 sequencer (Applied Biosystems) and alleles were calculated using GeneMapper 4.0.

Statistical analysis

The results obtained were statistically analysed. For all groups studied, the number of cases (N), the mean (X), median (M), range (min-max), lower and upper quartile (25q-75q) and standard deviation (SD) of the continuous parameters were calculated. The verification of the hypothesis of equality of means of individual samples was performed by ANOVA or for groups with heterogeneous variance or a small number of cases of non-parametric rank sum test, Kruskal-Wallis test (homogeneity of variance was checked by Bartlett's test) — marked *. $P \leq 0.05$ was considered statistically significant, and $0.05 < p < 0.1$ was taken as the possibility of a trend. Statistical analysis was performed using the statistical software packages Computer EPIINFO Ver. 3.5.2 (dated 17-12-2010). The analysis of multivariate (logistic regression) due to the presence of NAFLD among both groups (n = 309, 141 without NAFLD and 168 with NAFLD) was performed. For the analysis introduced: BMI 25 kg/m^2, waist circumference 84cm, WHR 0.8, testosterone 0.5ng/mL, SHBG 34nmol/L, FAI 5.5, E2/T 80, AST20 U/L, ALT19 U/L, LDL –C 112 mg/dL, HDL –C 55 mg/dL, TG 89 mg/dL, CRP 1.1 mg/L, glucose 85 mg/dL, insulin 5.5 μIU/L , HOMA 1.1, PCOS. Multivariate analysis was performed by using logistic regression (estimation quasi-Newton). P £ 0.05 was considered statistically significant,

Results

Women with PCOS and NAFLD had significantly higher BMI, WHR and waist circumference compared to women with PCOS without NAFLD and women without PCOS. In the group of women with PCOS and NAFLD, there was also observed significantly lower SHBG and lower value E2/T ratio, and a significantly higher FAI compared to the other groups (Table II).
AST concentrations in the investigated groups of women were not significantly different, while ALT levels were significantly higher in PCOS women with NAFLD compared to women with PCOS without NAFLD and women without PCOS. Women with PCOS both with and without NAFLD had significantly higher levels of fasting glucose and fasting insulin and HOMA compared to women without PCOS. Among women with PCOS there

Table II. *Clinical and biochemical characteristics of PCOS women — subgroups with (1) and without non alcoholic fatty liver disease NAFLD (2) and women without PCOS with NAFLD (3)*

Tabela II. *Charakterystyka kliniczna i biochemiczna kobiet z PCOS — podgrupa (1) z niealkoholowym stłuszczeniem wątroby, bez NAFLD (2) oraz kobiety bez PCOS z NAFLD (3)*

	PCOS women with NAFLD (1)				PCOS women without NAFLD (2)			NAFLD controls (3)*				
	N = 106				N = 76			N = 62				
	M	IQ	uQ	p	M	IQ	uQ	M	IQ	uQ	1 *vs.* 3	2 *vs.* 3
WHR	0.83	0.78	0.91	***	0.781	0.749	0.853	0.789	0.745	0.862	***	ns
WC [cm]	88.0	77.0	102.0	***	76.0	71.0	85.8	79.5	72.0	4.0	*	*
Testosterone [ng/mL]	0.58	0.43	0.82	ns	0.52	0.35	0.68	0.386	0.260	0.510	***	***
SHBG [nmol/L]	28.5	18.6	44.4	***	38.0	25.0	60.8	39.9	29.3	60.4	***	ns
FAI	7.25	4.49	11.22	***	5.28	2.80	8.00	3.02	1.98	5.39	***	**

*p < 0.05; ** p < 0.001; *** p < 0.0001; ns — not significant; BMI — body mass index; WHR — waist-to-hip ratio; WC — waist circumference; SHBG — sex hormone binding globulin; FAI — free androgen index; data is presented as M (median) and lower quartile (IQ) and upper quartile (uQ)

Table III. *Biochemical characteristics of PCOS women — subgroups with (1) and without non alcoholic fatty liver disease NAFLD (2) and women without PCOS with NAFLD (3)*

Tabela III. *Charakterystyka biochemiczna kobiet z PCOS — podgrupa (1) z niealkoholowym stłuszczeniem wątroby, bez NAFLD (2) oraz kobiety bez PCOS z NAFLD (3)*

	PCOS women with NAFLD (1)				PCOS women without NAFLD (2)			NAFLD controls (3)*				
	N = 106				N = 76			N = 62				
	M	IQ	uQ	p	M	IQ	uQ	M	IQ	uQ	1 *vs.* 3	2 *vs.* 3
ALT[IU/L]	21	15.0	36.0	***	16.0	13.0	22.0	18.0	13.0	24.0	**	ns
AST[IU/L]	21	17.0	27.0	ns	20.0	17.0	24.0	20.0	16.0	23.0	**	ns
fGlucose[mg/dL]	86.5	81.5	92.0	***	81.0	78.0	86.0	75.6	75.0	87.0	***	ns
fInsulin[mIU/mL]	6.28	2.64	13.7	**	4.14	2.00	8.79	2.89	2.00	7.65	**	ns
HOMA-IR	1.24	0.50	3.02	**	0.78	0.41	1.98	0.50	0.41	1.56	*	ns
HDL-chol[mg/dL]	52.0	40.5	65.5	***	62.0	49.0	74.0	65.5	47.0	86.0	***	ns
Triglyceride[mg/dL]	120.0	67.0	152.5	**	75.7	57.0	101.0	69.5	53.0	94.0	***	ns

*p < 0.05, ** p < 0.001; *** p < 0.0001; ns — not significant; ALT — alanine aminotransferase; AST — aspartate aminotransferase; f Glucose — fasting glucose; f Insulin — fasting insulin; HOMA-IR — homeostasis model assessment-insulin resistance index; data is presented as M (median) and lower quartile (IQ) and upper quartile (uQ)

were significantly higher triglycerides and lower HDL-C compared to women without this disease. The values of the parameters are shown in Table III. Logistic regression showed that all of the analysed factors influence NAFLD, but BMI > 25 kg/m^2, E2/T < 80, ALT > 19 U/L, glucose > 85 mg/dL were independent factors ($\chi^2$4 = 182,5, p = 0.00000) as shown in Table IV. PCOS influenced NAFLD but was not an independent factor.

The studied groups were evaluated for lipoprotein lipase gene polymorphisms rs328 and rs268. There was no evidence that the evaluated polymorphisms influenced hepatic steatosis in PCOS women or in the group of women without PCOS. Comparing rs268 polymorphism, it was found that women with PCOS and NAFLD and without NAFLD AA genotype had a significantly lower frequency compared to women without PCOS. The test results are shown in Table V.

Discussion

Women with PCOS are well known to have a higher prevalence of obesity, insulin resistance and dyslipidemia, which are common risk factors for NAFLD and metabolic syndrome. Therefore they have also been reported to have a higher prevalence of NAFLD [10, 16, 17]. Our data confirms the prevalence of obesity in PCOS women, especially in women with PCOS and NAFLD. Performed multivariate analysis showed that body mass index

Table IV. *Independent factors influencing nonalcoholic fatty liver disease in multivariate analysis (logistic regression)*
Tabela IV. *Niezależne czynniki wpływające na wystąpienie niealkoholowego stłuszczenia wątroby na podstawie analizy wieloczynnikowej*

	Estimate	p	OR	–95% CI	+95% CI
BMI > 25 kg/m²	1.08	0.00007	2.94	1.74	4.98
E_2/T	-0.593	0.0274	0.553	0.327	0.936
ALT > 19 U/L	0.526	0.0471	1.69	1.01	2.85
f Glucose > 85 mg/dL	0.534	0.0326	1.74	1.05	2.89

P < 0.05 statistically significant; OR — odds ratio; CI — confidence interval; ALT — alanine aminotransferase; f Glucose — fasting glucose; BMI — body mass index

Table V. *Genotype and allelic frequencies of rs268 lipoprotein lipase gene polymorphisms*
Tabela V. *Genotyp i częstość alleli polimorfizmu rs268 genu lipazy lipoproteinowej*

	PCOS with NAFLD (1) N = 70	P 1 *vs.* 2	Controls with NAFLD (2) N = 52	P 2 *vs.* 3	PCOS without NFLD (3) N = 42	P 1 *vs.* 3
Allele frequency	14A/126G	0.0440	22A/82G	0.0311	5A/79G	0.121
rs268-AA	2 (85%)		8 (15.38%)		0 (0.00%)	
rs268-AG	10 (14.28%)		6 (11.53%)		6 (14.29%)	
rs268-GG	58 (2.85%)		38 (73.08%)		36 (85.71%)	

> 25 mg/m² is an independent factor influencing NAFLD in women. Our results do not confirm the observation of other authors that NAFLD in women with PCOS is more frequent than in women without PCOS. The prevalence of NAFLD in PCOS women ranges from 30 to 60% [18, 19]. Among our patients with PCOS, 57% had NAFLD, but in healthy controls NAFLD was observed in 49%. In the whole group with NAFLD, (n = 168) there were 106 PCOS women and 72 women without PCOS; in the group without NAFLD (n = 141), 78 had PCOS and 63 were healthy controls. NAFLD was more frequent in PCOS women but the difference was statistically not significant (p = 0.204).

In the present study, we found that women with PCOS and NAFLD had significantly higher levels of ALT and FAI and significantly lower E2/T ratio than PCOS women without NAFLD and healthy controls. ALT is a sensitive indicator of liver cell injury and levels of ALT are sensitive in the detection of NAFLD in obese and non-obese patients [20, 21]. However, ALT levels can be normal in patients with clinical or histological manifestations of NAFLD [22, 23]. There have been recent suggestions that the upper limit of normal for serum ALT needs to be lowered from 40 U/L to 30 U/L for men and 19 U/L for women [24]. The levels of ALT in our patients were within the normal laboratory range, although in PCOS women with NAFLD they were significantly higher than in PCOS without NAFLD and in controls. Our data shows that ALT > 19 U/L is an independent factor influencing NAFLD. The androgen excess in women with PCOS might contribute to the aggravation of obesity-related liver cell injury. It is known that women with PCOS have greater BMI than controls and that elevated ALT exists in both obese and non-obese PCOS women [22]. Our data confirms these observations. Chen et al. observed that elevated level of ALT in relation to the presence of PCOS was independent of the effects of age, obesity, high triglycerides, high plasma glucose and LDL levels and was positively associated with androgen level.

In our study, PCOS women with NAFLD had significantly higher FAI and lower E2/T ratio than PCOS women without NAFLD and than controls. Hyperandrogenemia in PCOS may be one of the most important factors for elevation of ALT, due to steatosis but also due to a direct hepatotoxic effect of androgens unrelated to NAFLD. It is known that hyperandrogenism is associated with the polycystic ovary morphology in women with PCOS and can influence the development of metabolic syndrome, dyslipidemia and insulin resistance independent of obesity in this group of women [9, 25]. The results of our study show E_2/T ratio < 80 to be an independent factor of NAFLD. We also observed that the women with PCOS with NAFLD had significantly higher fasting glucose, fasting insulin levels and HOMA index than PCOS women without NAFLD and women without PCOS. Our results suggest that a fasting glucose level > 85 mg/dL could be an independent factor influencing NAFLD. Taken together, these findings support the suggestion that hyperandrogenism influences the metabolic features in PCOS.

PCOS, one might say, is an ovarian manifestation of metabolic syndrome.

Hepatic lipase is required for the normal metabolism of LDL, and there is increasing evidence that genetic variation in hepatic lipase activity leads to variation of the plasma concentrations of some apolipoprotein B containing-lipoproteins, and in the physiochemical properties of LDL. To date, most studies of hepatic lipase polymorphism have focused on normolipidemic individuals [26, 27].

Occurrence of LPL polymorphisms depends on the type and the study population. The incidence of rs328 polymorphism ranges from 9.6 to 20% of the total population, while in people with heart disease it is significantly lower at 3%. This polymorphism increases LPL activity, modifying the lipid metabolism and leading to an increase in HDL-C, and lower TG and LDL-C [27]. In our studies, we found no association of polymorphism rs328 LPL with NAFLD in women with and without PCOS. Polymorphism rs268 encourages the formation of lipid disorders, which occur significantly more often in patients with reduced HDL-C and elevated TG. Conversion of two amino acids has a significant impact on the activity of LPL, lowering it. When TG grows by 20%, HDL-C decreases by 0.8 mmol/L and the risk of heart disease increases 1.4 times [28]. For this polymorphism, we found no significant difference among the subjects. We observed only significantly less frequent allele AA of rs268 polymorphism in women with PCOS with and without NAFLD compared to the women without PCOS. Unfortunately, these observations do not allow us to draw conclusions — whether, for example, is it associated with hyperandrogenism — due to the relatively small group size, and it needs further investigation.

Conclusions

PCOS is not an independent factor influencing NAFLD in women. The influences on NAFLD incidence in women are BMI > 25kg/m^2, glucose level > 80 mg/dL, E2/T < 80 and ALT > 19IU/L as independent factors. It is probable that hyperandrogenism in PCOS may increase the risk of NAFLD indirectly by obesity, insulin resistance, and directly by the hepatotoxic effect. Polymorphisms rs328 and rs268 of the lipoprotein lipase gene do not affect the occurrence of NAFLD in women with PCOS or without PCOS.

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