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Obesity Related Lipid Profile and Altered Insulin Incretion in Adolescent with Policystic Ovary Syndrome

Annamaria Fulghesu and Roberta Magnini
Department of Obstetrics and Gynecology, University of Cagliari, Cagliari, Italy

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder, present in 5 – 7% of women of reproductive age. The diagnosis of PCOS was made according to Rotterdam criteria in presence of at least two of the following: 1) oligomenorrhea and/or anovulation; 2) hyperandrogenism (clinical and/or biochemical); 3) polycystic ovaries with the exclusion of other etiologies (1). The disorder is characterized by irregular menstrual cycle, chronic anovulation and hyperandrogenism. Women with PCOS demonstrate marked clinical heterogeneity: the commonly associated features of hirsutism, acne, polycystic-appearing ovaries, obesity and acanthosis nigricans are neither uniform nor universal (2-3). In time the disorder may lead to onset of hyperinsulinemia, insulin resistance, gestational diabetes, early onset of type 2 diabetes mellitus (DM), dyslipidemia and cardiovascular disease (CVD) (4-5).
PCOS is characterized by a complex physiology implicating an interaction with environmental and genetic factors, resulting in a broad spectrum of reproductive and metabolic disorders. (6-7) Adult females with PCOS may be at increased risk for atherosclerotic cardiovascular disease (CVD) due to increased prevalence of obesity and central adiposity as well as to hypertension, hyperinsulinemia, type 2 DM, and dyslipidemia in these patients (8).The prevalence of obesity and consequently the presence of metabolic abnormalities reported in Italian and American published studies differs considerably, underlining the presence of important ethnic differences. (9, 10, 11, 12).
A percentage ranging from 30-75% of women with PCOS are obese, European women generally weighing less than their American counterparts (20,21). Hyperinsulemia and/or insulin resistance (IR) are frequently manifested in obese, and to a lesser extent (50%) in lean, PCOS patients (3, 13, 14). Hyperandrogenaemia, hyperinsulemia and obesity are considered as risk factors for the development of hypertension and dyslipidemia, diabetes mellitus and coronary disease in PCOS (15-16). The causes of metabolic disorders in PCOS remain to be clarified, but include obesity-related IR, an intrinsic abnormality of postreceptor insulin signaling (e.g. excess serine phosphorylation), and abnormal insulin secretion. On the other hand, increased resistance to insulin is a hallmark of the onset of normal pubertal development with natural to pre-pubertal values at the end of puberty in non-obese subjects. Consequently, in early adolescence a physiological resistance to insulin should be taken into account (12).

Dyslipidemia in PCOS is frequently manifested and is characterized by elevated plasma levels of low- density lipoproteins (LDL), very-low-density lipoproteins (VLDL) and triglycerides with concomitantly reduced concentration of high-density lipoproteins (HDL) in obese subjects (17, 18). A decrease in HDL, rise in triglyceride, VLDL, and LDL levels, as well as qualitative disorders of the LDL have all been described in young and adult PCOS (19). Moreover, recent data have shown a higher prevalence of metabolic syndrome in adolescent PCOS compared to controls (20) as well as an early impairment of endothelial structure and function even in non-dyslipidemic subjects with PCOS syndrome (21). Nevertheless, metabolic disorders in PCOS have not been extensively studied in the adolescent population. Several studies have shown how both lean and obese adolescents with PCOS appear to present an increased risk of both metabolic disorders and impaired glucose tolerance and diabetes (22), similar to their adult counterparts. A previous study carried out by our group demonstrated that the Italian young PCOS population is characterized by a high incidence of insulin alterations also in presence of normal weight and normal peripheral insulin resistance (12). Although the prevalence of dyslipidemia differs between PCOS subjects and young healthy girls, it however remains to be clarified whether dissimilarities in dyslipidemia occur in relation only to BMI or also to alterations to the insulinmetabolism and/or hyperandrogenemia.

Carmina recently demonstrated that MBS in women with PCOS is less common in Southern Italy compared to rates reported in the USA, the former reaching only 8.2% compared to a prevalence of 43-46% reported by US authors (23). The prevalence of MBS in the adult Italian PCOS population is higher than in control population matched for BMI, suggesting that body weight may be only in part responsible for this metabolic disorder (24).

Although few studies have investigated the latter condition in adolescents, it could prove to be of considerable importance in view of the health implications involved, requiring medical counseling to implement an adequate change in lifestyle. Likewise, obesity rate in adolescent PCOS subjects differs between Europe and the USA. In Sardinia, the incidence of obesity is lower than throughout the rest of Italy, with only 3-4% of high school female population presenting a BMI >25 (25). A combination of genetic factors, different lifestyle and diet are likely involved. In view therefore of the regional peculiarity, the patient population attending our Clinic was deemed to be of interest.

Therefore it is important to understand the relationship between lipid pattern and BMI, hyperinsulinemia and/or insulin resistance and circulating androgens in adolescent PCOS. In a study carried out in July 2005 to the Adolescent Center for gynecological diseases of the Department of Obstetrics and Gynecology, University of Cagliari, San Giovanni di Dio Hospital seventy-one adolescent (age 13-18) subjects affected by PCOS were recruited for this study. On the basis of the various aspects linking PCOS dyslipidemia and CVD risk, the present study was designed to investigate the influence of BMI and insulin metabolism derangement on lipid levels. All subjects were screened for other causes of hyperandrogenism, such as androgen secreting tumors and congenital adrenal hyperplasia (tested by evaluation of 17- dydroxyprogesterone). All subjects were euthyroid and devoid of hyperprolactinemia, diabetes mellitus and cardiovascular disease. No subjects had taken hormonal contraceptives or other type of medication or been on a diet that may have affected lipid profile, carbohydrate metabolism or insulin levels for at least 3 months preceding the study. No subjects were either smokers or drinkers. No subjects practiced sports on a regular basis (3 or more 20-min sessions of aerobic exercise per week).

These patients were linked with a control group consisting of healthy patients referred to the Adolescent centre for ultrasound screening of ovarian disease.
Control subjects and PCOS were studied 5 to 8 days following menstrual bleeding, which was progestin-induced in amenorrhoic patients. All patients were studied at least 15 days following Medrossi-Progesteron-Acetate administration (MAP 10 mg for 5 days). At the time of admittance to the study the presence of a dominant follicle, recent ovulation, or luteal phase was excluded by ultrasound examination and serum P evaluation. Height and weight were measured on the morning of testing. Waist and hip circumference were measured as previously referred. Blood pressure was measured in the second position and in the right arm (26) after 15 minutes resting.The hormonal study (after 12 hours overnight) included baseline plasma determination of LH, FSH, Estradiol (E2), Androstenedione (A), Testosterone (T), Dehydroepiandrosteronesulphate (DHEAS), 17hydroxyprogesterone (17-OHP) and Sex-hormone-binding globulin (SHBG). Lipid assay was performed to measure total cholesterol level, high-density lipoprotein cholesterol level (HDL), low-density lipoprotein cholesterol level (LDL) and triglyceride level. Homocysteine levels were also determined.
Adolescents meeting three or more of the following criteria were diagnosed with MBS: waist circumference of at least 90th percentile for age and gender; systolic or diastolic blood pressure at least 90th percentile for age, height and gender; fasting TG at least 110mg/dl (90th percentile for age); fasting HDL not exceeding 40mg/dl (10th percentile for age); and fasting glucose at least 110mg/dl.
Subsequently, patients underwent a 75-g oral glucose tolerance test (OGTT). Insulin, C-peptide, and glucose serum concentrations were analyzed prior to (time 0) and 30, 60, 90, 120 and 180 min after oral glucose load. A normal glycemic response to OGTT was defined according to the criteria of the National Diabetes Data Group (27). Insulin, C-peptide and glucose response to glucose load were expressed as area below the curve (AUC), calculated according to the trapezoidal rule. The homeostatic index of IR (HOMA) was calculated as follows: HOMA = [fasting insulin (μU/ml) x fasting glucose (mmol/L/22, 5)]. (28) The body mass index (BMI) was calculated according to the following formula: body weight in kilograms/ height in m2. Normal weight was considered as $18 \leq BMI \geq 25$. The degree of hirsutism was quantified using Ferriman and Gallwey (F-G) score (28).
No differences were observed with regard to the presence of overweight and obese subjects between PCOS and controls (30% vs. 23%); a similar finding was obtained also for waist measurement and WHR, confirming that obesity is not a common finding in young PCOS subjects in the population studied.Moreover, no subjects affected by metabolic Syndrome or diabetes either among PCOS or in the control group were detected. No differences were revealed in lipid levels between PCOS and controls. In addition, no differences were reported for any of the fasting metabolic parameters (i.e. Glucose fasting insulin, HOMA ratio), whilst a higher insulin response under OGTT was obtained for PCOS subjects. On the other hand, statistical correlations clearly demonstrated the influence produced by BMI and waist measurement on HDL, triglyceride and LDL levels. However, dividing the population into tertiles for BMI and waist measurement significant differences were revealed for both HDL and LDL levels in lean overweight and obese subjects and in relation to the presence of visceral fat.The above features have also been reported by several authors carrying out studies on young subjects.
Glueck published a study regarding PCOS and regular cycling adolescents in USA demonstrating a higher prevalence of obesity and dyslipidemia in PCOS.

However, when subjects were matched one-by-one for BMI and age, differences in lipids were no longer significant. In a recent paper on young obese subjects Shroff failed to demonstrate any difference in lipid as well as traditional CV factors in PCOS and control populations, but demonstrated a higher BMI in subjects presenting subclincal coronary atherosclerosis (CAC) (10). In young subjects from southern Italy, Orio demonstrated normal lipid levels in lean PCOS even in the presence of increased dimensions of heart ventricles.The above findings all seem to indicate that rather than being an insulin-correlated factor BMI may well be implicated in lipid alteration. On the other hand, the presence of increased waist measurements in PCOS population suggests that the presence of visceral fat may represent an additional risk factor, independent from BMI in PCOS. The influence of insulin on lipid profile was also determined.

Indeed, to date very few authors have investigated this aspect: Mather found a significant increase in traditional CV risk factors in PCOS women with fasting hyperinsulinemia in respect to their normoinsulinemic counterparts; this difference persisted when BMI was included as covariate. (29) Through reduction of hyperinsulinemia by means of metformin treatment Banazewska obtained a significant increase of HDL and reduction of triglycerides in a group of 43 adult PCOS. Our group recently published a paper on the peculiar insulin derangement observed in a population of normal weight young PCOS demonstrating a low incidence of insulin resistance but high incidence of hyperinsulinemia under OGTT (30). This peculiar metabolic alteration was confirmed in the present sample, thus allowing the separation of hyperinsulinemia from peripheral insulin resistance in data analysis.

Ibanez et al. also demonstrated higher serum insulin levels after OGTT with normal insulin sensitivity in a population of adolescent girls with PCOS. The causes underlying the increased response of β-cells in these subjects are, as yet, unknown. It is not clear whether high levels of insulin necessarily indicate the presence of a disorder although it may be hypothesized that adaptation to the chronic risk of hypoglycemia in hyperinsulinemic subjects could lead to IR after some time. Moreover, our group recently demonstrated that a normal HOMA score is not sufficient to exclude earlymetabolic abnormalities such as hyperinsulinemia in young lean PCOS subjects. Hyperinsulinemia per se could contribute toward onset of hyperandrogenism independently of peripheral IR.(12)

In this study was found a significant negative correlation between HDL and fasting insulin and HOMA, but this correlation was no longer significant when the influence of BMI was excluded, whereas insulin AUC was not related to any lipid parameters.

Furthermore, although the PCOS sample studied here was divided into tertiles on the basis of both insulin resistance and insulin AUC levels, the data obtained clearly indicate the failure to detect any relationship between insulin levels and lipid profile. Nevertheless, surprisingly a positive correlation was observed between A levels and HDL and a negative correlation between A and triglycerides. Reports present in literature did not afford any explanation for this result. A negative effect of A on HDL levels has previously been reported in males to whom A supplements had been administered (31). Moreover, exogenous T is reported to influence negatively HDL via hepatic lipase (HL) (31) an enzyme that increases the clearance of HDL. Less is known about the regulation of HDL by endogenally-derived androgens. A study performed in women with PCOS was not able to demonstrate any correlation between T and HDL. Considerable controversy exists as to the effect of androgens on lipoprotein lipase (LPL) activity.

In obese women LPL activity correlated positively with plasma free testosterone (32), whereas in women with PCOS a correlation with LPL activity was demonstrated.

Other authors have attributed to coexisting (29) insulin resistance the negative effect of androgen observed on lipid profile. In this case, the low incidence of insulin resistant subjects in a population may explain this unexpected result.
In conclusion, no lipid differences were revealed between our population of adolescent PCOS from southern Italy and controls.
Anthropometric characteristics (BMI, waist measurement and WHR) are the main parameters correlated to lipid derangement, confirming the importance of treating obesity at an early age to prevent onset of complex metabolic syndromes in the future. The latter may be of particular importance in PCOS populations in which insulin alterations (hyperinsulinemia and insulin resistance) are well known peculiarities potentially capable of influencing the long-term evolution of this endocrine disorder towards CVD and diabetes mellitus. A targeted support program should be set up for these young patients aimed at altering life style with the specific aim of reducing BMI and preventing onset of dyslipidemia.

	PCOS (n°71)	**CONTROLLI (n°94)**	**P**
Age (years) (M±ES) (range 13-19)	18,61 ± 0,4	18,10 ± 0,38	NS
BMI (kg\m²) (M±ES)	23,97 ± 0,72	22,56 ± 0,50	NS
Overweight (BMI 25 - 29) (%)	10%	11%	
Obesity (BMI > 29) (%)	20%	13%	
Waist (cm) (M±ES)	78,60 ± 1,79	75,56 ± 1,18	NS
WHR (M±ES)	0,77 ± 0	0,77 ± 0	NS
Hirsutism (score F&G) (M±ES)	11,24 ± 0,67	6,7 ± 0,45	0,005°
LH (IU/L)(M±ES)	5,21 ± 0,55	4,19 ± 0,36	NS
FSH (IU/L)(M±ES)	6,42 ± 0,63	5,96 ± 0,19	NS
E_2 (pmol/L)(M±ES)	129,30 ± 20,58	136,81 ± 13,25	NS
A (nmol/L)(M±ES)	0,08 ± 0	0,05 ± 0	0,005°
Tot T(nmol/L)(M±ES)	0,02 ± 0	0,01 ± 0	0,005°
17OHP (ng/mL)(M±ES)	1,49 ± 0,18	1,18 ± 0,07	NS
DHEAS (µmol/L)(M±ES)	2,05 ± 0,12	1,6 ± 0,09	NS
SHBG (nmol/L)(M±ES)	65,83 ± 4,54	71,18 ± 3,35	NS

°P < 0,05

Table 1. Shows the clinical and hormonal characteristics of PCOS population vs. Control group. No significant differences were revealed in age, body weight, waist and WHR between PCOS and control group. Likewise, no differences were observed in the incidence of overweight or obesity in the two groups. As expected, the prevalence of hirsutism and circulating androgen levels were higher amongst PCOS.

	PCOS (n° 71)	CONTROLLI (n°94)	P
Fasting Glucose (mmol/L)(M±ES)	81,13 ± 0,65	88,00 ± 3,27	NS
Fasting Insulin (pmol/L)(M±ES)	119,98 ± 6,14	96,68 ± 4,73	NS
HOMA (M±ES)	61,02 ± 3,09	57,81 ± 2,41	NS
I-AUC 180 min (UI/ml)(M±ES)	21069 ± 978,39	16578 ± 729,37	0,05°
Cholesterol (mg/dl)(M±ES)	166,48 ± 3,53	169,51 ± 2,62	NS
HDL-Cholesterol (mg/dl)(M±ES)	54,26 ± 1,44	51,25 ± 0,89	NS
LDL-Cholesterol (mg/dl)(M±ES)	96,78 ± 3,08	104,55 ± 2,34	NS
Cholesterol/ HDL (mg/dl)(M±ES)	3,16 ± 0,09	3,37 ± 0,07	NS
Triglycerides (mg/dl)(M±ES)	73,91 ± 3,75	78,35 ± 3,86	NS
Homocysteine (µmol/L) (M±ES)	8,16 ± 0,20	7,68 ± 0,25	NS
PCR (M±ES)	2,04 ± 0,36	0,89 ± 0,11	NS

° P < 0,05

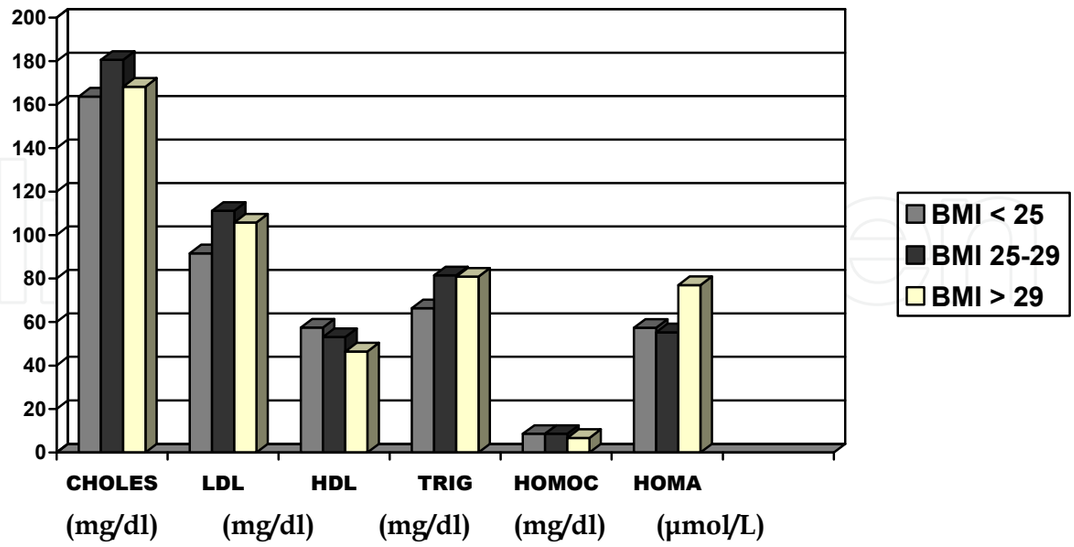
Table 2. Reports the metabolic features of PCOS and control group. Fasting metabolic indexes detected for glucose, insulin and HOMA were similar between the two groups. On the contrary, insulin secretion after glucose load (I-AUC) was significantly higher in PCOS subjects. Total cholesterol, HDL, LDL, triglycerides and homocysteine levels did not differ between PCOS and control groups

	Cholesterol	LDL-Cholesterol	HDL-Cholesterol	Triglycerides
BMI (kg\m²)	R = 0,0727	R = 0,2579·	R = - 0,404▪	R = 0,1576
WAIST (cm)	R = 0,0869	R = 0,2960·	R = - 0,5934▪	R = 0,1704
WHR (cm)	R = 0,1645	R = 0,2872·	R = - 0,1853	R = 0,1362
A (nmol/L)	R = 0,0136	R = - 0,0523	R = 0,3705▪	R = -0,2948·
Tot T (nmol/L)	R = - 0,1016	R = - 0,0948	R = 0,0012	R = - 0,0157
FSH (mIU/L)	R = - 0,0134	R = - 0,0143	R = 0,0623	R = - 0,0687
E2(pmol/L)	R = - 0,1011	R = - 0,0895	R = 0,0698	R = - 0,1984
DHEAS (µmol/L)	R = - 0,0498	R = - 0,0022	R = - 0,0447	R = - 0,0441
HOMA	R = 0,0762	R = 0,1770	R = -0,3335	R = - 0,0214
I-AUC 180 min(UI/ml)	R = - 0,0098	R = - 0,0272	R = - 0,0701	R = - 0,0287
SHBG (nmol/L)	R = - 0,0689	R = - 0,1514	R = 0,1102	R = 0,1013
17OHP (nmol/L)	R = 0,0418	R = 0,0582	R = 0,0854	R = - 0,1720
Homocysteine (µmol/L)	R = - 0,0670	R = - 0,0786	R = 0,0463	R = - 0,1108▪
Fasting Glucose	R = 0,0049	R = 0,0260	R = -0,0829	R = 0,0643
Fasting Insulin	R = 0,0586	R = 0,1557	R = -0,3314	R = -0,0174

P < 0,05
P < 0,01
P < 0,001

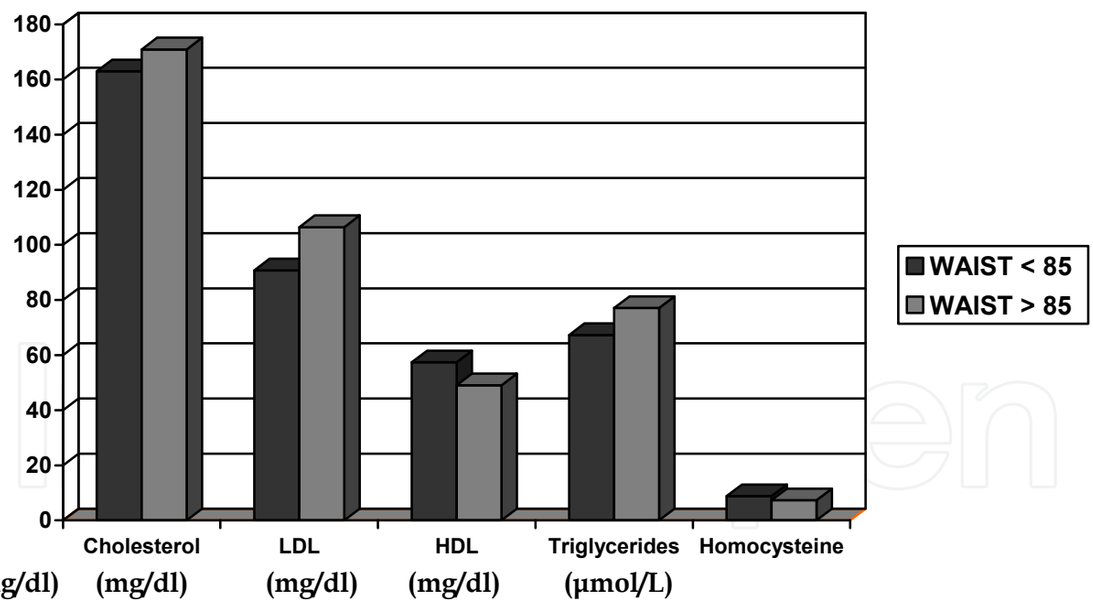
Table 3. Illustrates linear regression relationship featured between lipid and physical, hormonal and metabolic parameters. Total cholesterol levels were significantly related to WHR but not to other antropometric parameters. On analyzing cholesterol fractions LDL levels were found to correlate positively with BMI, Waist, WHR and HOMA but not with I-AUC. HDL results correlated in a markedly negative manner with the same physical parameters as BMI, WHR and waist circumference. Moreover, HDL was negatively correlated with both fasting insulin and HOMA but not I-AUC. Finally, HDL was positively correlated with circulating A and negatively with circulating T levels.
Triglycerides appeared to correlate positively with BMI, Waist and WHR, and negatively with A levels. Homocysteine levels correlated positively with plasma triglyceride content. In view of the potential capacity of BMI to affect insulin sensitivity, conditional regression analysis was performed on HOMA and lipid assays to exclude any possible influence of BMI: HOMA resulted as being no longer correlated with any lipid parameter.To determine whether lipid alterations were primarily caused by increased BMI, lipid assay was repeated stratifying the population into 3 weight categories: normal weight, overweight and obese, and waist measurements were classified (normal and excessive).

BMI (kg\m²)



P < 0,05 LDL BMI < 25 VS BMI 25-29
P < 0,05 LDL BMI < 25 VS BMI > 29
P < 0,05 HDL BMI < 25 VS BMI > 29

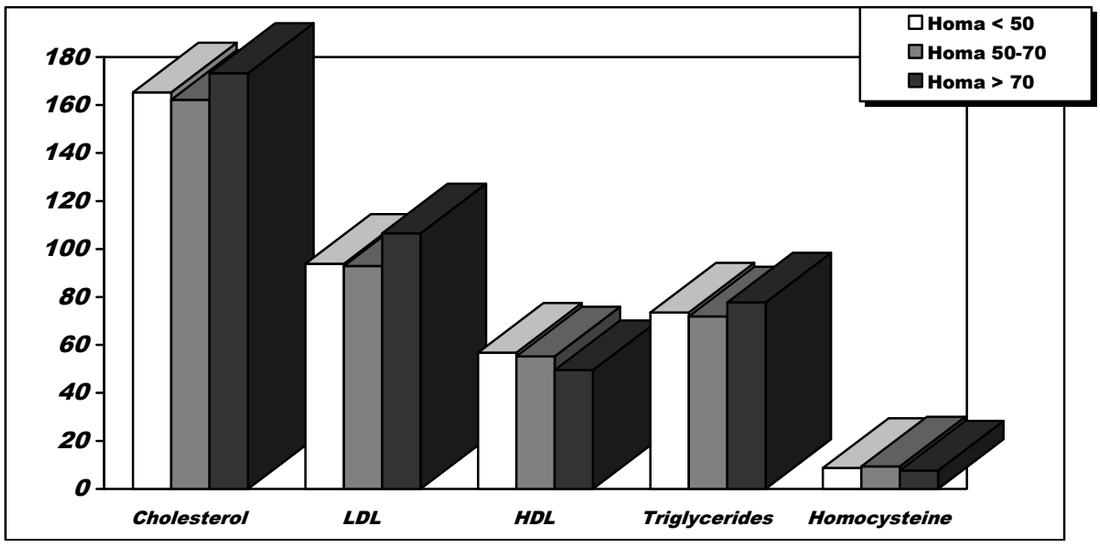
WAIST (cm)



P < 0,05 LDL WAIST < 85 VS LDL WAIST > 85
P < 0,05 HDL WAIST <85 VS HDL WAIST > 85

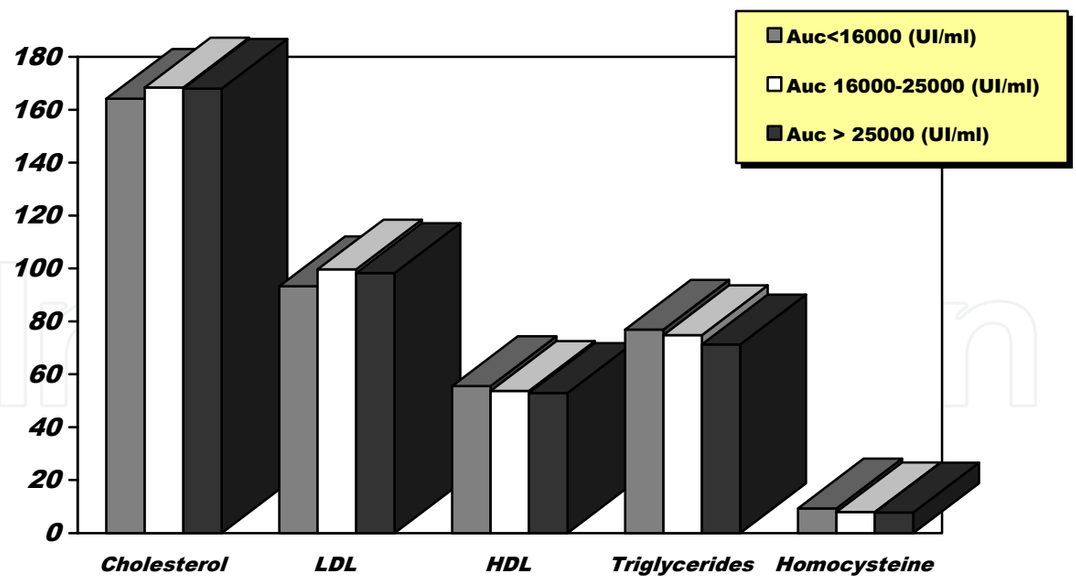
Fig. 1. Shows the lipid levels in relation to the BMI and the waist of PCOS group.Normal weight and normal waist subjects featured lower LDL and Higher HDL compared to increased waist overweight or obese counterparts. On the other hand, in order to evaluate the influence of metabolic alteration subjects were also stratified on the basis of both HOMA and Insulin AUC values (fig.2).

HOMA



(mg/dl) (mg/dl) (mg/dl) (mg/dl) (µmol/L)

I-AUC (UI/ml)



(mg/dl) (mg/dl) (mg/dl) (mg/dl) (µmol/L)

Fig. 2. Shows lipid levels in subjects divided into tertiles for both HOMA and Insulin AUC levels. Similar lipid values were demonstrated in all subjects.

	Cholesterol	LDL-Cholesterol	HDL-Cholesterol	Triglycerides
BMI (kg\m²)	R = 0,0800	R = - 0,0017	R = - 0,4762▪	R = 0,6962
WAIST (cm)	R = 0,1410	R = 0,0753	R = - 0,4253▪	R = 0,6765
WHR (cm)	R = 0,0326	R = - 0,1535	R = - 0,1878	R = 0,4262
A (nmol/L)	R = - 0,1921	R = - 0,0280	R = - 0,1845	R = 0,0007
Tot T (nmol/L)	R = - 0,3425	R = - 0,4544▪	R = - 0,1377	R = 0,3692
FSH (IU/L)	R = 0,3094	R = 0,3909▪	R = 0,3711▪	R = - 0,1603
E2(pmol/L)	R = 0,0150	R = 0,0124	R = - 0,0264	R = - 0,0876
DHEAS (µmol/L)	R = 0,1230	R = 0,1925	R = - 0,1793	R = 0,2206
SHBG (nmol/L)	R = - 0,2226	R = - 0,2834	R = 0,0655	R = - 0,0942
17OHP (nmol/L)	R = - 0,0925	R = - 0,0586	R = 0,1667	R = - 0,3703▪
HOMA	R = 0,4724	R = 0,5140	R = 0,2293	R = - 0,0123
I-AUC 180 min(UI/ml)	R = - 0,0021	R = 0,0331	R = - 0,3391	R = 0,2882
Homocysteine (µmol/L)	R = 0,2148	R = 0,1214	R = - 0,2604	R = 0,5656▪
Fasting Glucose	R = 0,0440	R = 0,1325	R = - 0,1952	R = - 0,0396
Fasting Insulin	R = 0,1226	R = 0,1315	R = 0,0435	R = 0,0972

P < 0,05
P < 0,01
P < 0,001

Table 4. Linear relationships between lipid assays and phisical endocrine and metabolic parameters in CONTROLS.

	Cholesterol	LDL-Cholesterol	HDL-Cholesterol	Triglycerides
BMI (kg\m²)	R = 0,1058	R = 0,2252	R = - 0,3930	R = 0,2933
WAIST (cm)	R = 0,1298	R = 0,2624	R = -0,3756	R = 0,2856
WHR (cm)	R = 0,2174	R = 0,3039	R = - 0,1924	R = 0,2063
E2(pmol/L)	R = - 0,0912	R = - 0,0912	R = 0,0541	R = - 0,1495
A (nmol/L)	R = - 0,0401	R = - 0,0953	R = 0,2933	R = -0,2400
Tot T (nmol/L)	R = - 0,1848	R = - 0,2191	R = 0,0181	R = 0,0085
SHBG (nmol/L)	R = - 0,1260	R = -0,1973	R = 0,1038	R = 0,0368
Fasting Glucose	R = 0,0107	R = 0.0800	R = - 0,1425	R = -0,0092
Fasting Insulin	R = 0,0773	R = 0,1239	R = - 0,1960	R = 0,0109
HOMA	R = 0,1349	R = 0,2269	R = - 0,2800▪	R = 0,0021
I-AUC 180 min(UI/ml)	R = 0,0324	R = 0,0550	R = - 0,0930	R = 0,0123
Homocysteine (μmol/L)	R = 0,0764	R = 0,0209	R = - 0,0656	R = 0,2863▪

P < 0,05
P < 0,01
P < 0,001

Table 5. Linear relationships between lipid assays and phisical endocrine and metabolic parameters in all patients.

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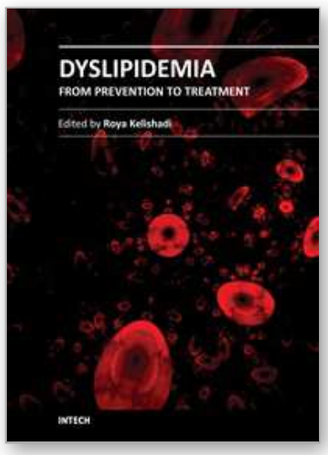

Dyslipidemia - From Prevention to Treatment
Edited by Prof. Roya Kelishadi

ISBN 978-953-307-904-2
Hard cover, 468 pages
Publisher InTech
Published online 03, February, 2012
Published in print edition February, 2012

Dyslipidemia has a complex pathophysiology consisting of various genetic, lifestyle, and environmental factors. It has many adverse health impacts, notably in the development of chronic non-communicable diseases. Significant ethnic differences exist due to the prevalence and types of lipid disorders. While elevated serum total- and LDL-cholesterol are the main concern in Western populations, in other countries hypertriglyceridemia and low HDL-cholesterol are more prevalent. The latter types of lipid disorders are considered as components of the metabolic syndrome. The escalating trend of obesity, as well as changes in lifestyle and environmental factors will make dyslipidemia a global medical and public health threat, not only for adults but for the pediatric age group as well. Several experimental and clinical studies are still being conducted regarding the underlying mechanisms and treatment of dyslipidemia. The current book is providing a general overview of dyslipidemia from diverse aspects of pathophysiology, ethnic differences, prevention, health hazards, and treatment.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Annamaria Fulghesu and Roberta Magnini (2012). Obesity Related Lipid Profile and Altered Insulin Incretion in Adolescent with Policystic Ovary Syndrome, Dyslipidemia - From Prevention to Treatment, Prof. Roya Kelishadi (Ed.), ISBN: 978-953-307-904-2, InTech, Available from: http://www.intechopen.com/books/dyslipidemia-from-prevention-to-treatment/obesity-related-lipid-profile-and-altered-insulin-incretion-in-adolescent-with-pcos

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Phone: +385 (51) 770 447
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InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
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