The Correlations Between ABO Blood Type and the Metabolic Disorders in Adolescents with Polycystic Ovarian Syndrome

MARIANA STUPARU CRETU[1,2], CAMELIA BUSILA[1,3]*, DOINA CARINA VOINESCU[1], GABRIELA BALAN[1]

[1] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, Centre of Research in Medical-Pharmaceutical Field, 35, Al. I. Cuza Str, 800010, Galati, Romania

[2] Buna Vestire Hospital of Obstetrics and Gynecology, 99 N.Alexandrescu Str, 800151, Galati, Romania

[3] Sf Apostol Ioan Emergency Hospital for Children, 2 Gh. Asachi Str, 800487, Galati, Romania

The Polycystic Ovary Syndrome (PCOS) represents a multidisciplinary medical desease due to its multiple phenotypes described and obtained as a result of various combinations of characteristic disorders: reproductive, metabolic and ovarian ultrasonographic image. The appearance of certain important complications in its evolution is possible by means of a correct management of this condition. Although the etiopathogeny of PCOS is not completely demonstrated, the early diagnosis implies the taking into consideration of the associated risk factors. The present study analyses the interdependency between the ABO blood types and the PCOS variable characteristics of a positive sample of 122 adolescents. Significant links between girls with O and B blood types and metabolic disorders have been demonstrated - some of them having protective connection and other ones as risk factors.

Keywords: ABO blood type, Polycystic Ovary Syndrome, adolescents, Metabolic Disorders

Among the 36 human identified blood type systems, the most important one is the ABO type [1]. The blood groupsremain unchanged throughout life,they are hereditary and are transmitted according to the laws of genetics. The locus of the allele genes which determine the ABO blood types groups is situated on the long arm of chromosome 9, band 3, sub-band 4 (9q34). The three allele genes of the system (A, B and O) determine four phenotypes: O(I), A(II), B(III) and AB(IV) [1]. The historic explanation of the appearance of ABO groups and the specific of the rate of all groups in a certain area of the Earth is linked to the migration of the ancient population and the selection of the mutations occurred in time. This fact was also demonstrated by the DNA study of ancient skeletons and of Egyptian mummies [2]. Being the oldest blood group, nearly 50% of the population has O blood type with a global average of 46%. The next is Ablood type with an average of 40%, B and AB groups with a lower rate of occurrence of 10%, respectively 4%. In Romania, the highest rate is that of A blood type (41%), followed by O type (34%), B type (19%) and AB type (6%) [3].

At present, approximately 7500 erythrocyte antigens divided into 9 systems have been identified, the most important ones in practicebeing A and B [4]. The antigens attached to the surface of the erythrocytes may be glycoproteins, carbohydrates or glycolipids. The main differences between the groups are due to the linking site of the antigen, O blood typebeing lacked by these antigens [5]. The ABO antigens are definitely present in the body on the surface of various cell types, leading to a series of researches which should prove the role of the ABO blood types in the pathogeny of various human disorders.

The lab blood tests is a common method of investigating a person and can direct medical staff to early diagnosis or the risks of a disease [6].Studies on the genetics of the ABO groups have also demonstrated the advantage or the susceptibility of some individuals to certain diseases depending on the presence or the absence of anti-A or anti-B antibodies. Thus, it has been demonstrated not only their importance in transfusionalpractice, but also the predisposition of the individuals with a certain blood type to some behaviours and diseases. Attempts have also been done on the interdependence between the antigens of the blood types and longevity [7] or various diseases: infectious diseases, e.g. a Plasmodium Falciparum, Helicobacter pylori, the HIV virus, Haemophylusinfluenzae, Escherichia coli, Pseudomonas aeruginosa or Vibrio cholerae[8], certain non-communicable diseases: susceptibility to arterial or venous thromboembolism[9], type 2 diabetes mellitus-(DM2)[10],cardio-vascular diseases[11], various types of cancer:pancreatic, gastric, skin, ovarian, pulmonary, colorectal, breast[12]. Various studies tried to prove the benefits of a certain diet specific to each group of blood, but other studies contradicted them [13].

Interdependencies between a certain blood type and problems linked to fertility or other specific genital disorders have also been searched: some studies have demonstrated a positive connection [14,15], while others have not [16].

The Polycystic Ovary Syndrome (PCOS) represents a studied disorder and it is often approached by various medical specialities.Although a definition unanimously accepted has not been formulated, the labelling criteria stated by the ESHRE-ASMR(European Society of Human reproduction and Embriology / AmericanSociety of Reproduction Medicine) specialists are still effectual. The illness is known as a diverse association of hyper-androgenismsigns with reproductive irregularities and ovary specific imagistic changes, starting early, in adolescence. Although neither its causes nor its origin have been completely explained, the specialists agree upon the complications which may occur in evolution:metabolic abnormalities (obesity, type 2 diabetes mellitus or gestational diabetes, metabolic syndrome), cardiovascular disease, reproductive problems (menstrual disorders, infertility, recurrent miscariage, endometrialtumor), mental problems (depression), accompanied by lowered self-esteem in most of the cases [17].A genetic study has identified 3 predisposing chromosomal loci for PCOS, on the 2p16.3, 2p21 and 9q33.3 chromosomes[18], chromosome 9 also having the locus for types ABO coding.

* email: camelia_busila@yahoo.com

There are few studies on the relationship between ABO types and PCOS and the results were inconclusive. An Iraqi study performed in 2011 emphasized onlya higher PCOS predisposition in women with O blood type [19]. A further Indian study showed just a high PCOS predisposition in women with O blood type followed by blood type B in what the rate is concerned [20]. Our study aims to assess whether any correlation may be done between the clinical and laboratory test changes in PCOS adolescents and their ABO system blood type in the South-Eastern area of Romania.

Experimental part

Material and methods

This research complies with the World Health Organization and European Union law concerning medical research on human subjects and was approved by the Ethic Committee of the Dunarea de Jos University from Galati.

The study was performed on a sample of 122 girls between 14 and 19 years old from the patients of Buna Vestire Obstetrics and GynecologyHospital and Sf. Apostol Ioan Children Emergency Hospital in Galati, Romania. The girls were diagnosed with PCOS according to the latest ESRE-ASMR criteria in 2012: clinical signs of hirsutism or the existence of biochemical hyper-androgenism+ anovulation / menstrual disorders + polycystic ovarian ultrasound aspect [17]. The blood type frequency have been compared with a sample group of 102 non-PCOS girls and a Romanian rate.

The protocol has shown the results of different parameters, as well as the statistics analysis of the correlations between them. Aspects connected to the occurrence of the three definition criteria have been mainly considered:hyperandrogenism (HA) + menstrual disorders + polycystic ovarian ultrasound aspect and after wards the PCOS sample group has been selected.

All the girls have been subject to a complete detailed anamnesis, clinically and ultrasound examined and specific laboratory tests have been performed. Anthropometric data have been marked for a better assessment of the adipose tissue disposal: waist circumference (WC), hip circumference (HC) and body mass index (BMI) - as the ratio between weight and height [2] adequate forage percentiles for girls. All the values andthe weight classes were interpreted according toCenters for Disease Control and Prevention criteria. For BMI,onedefines: Obesity ≥ 95thpercentile; Overweight =85-95thpercentile; Normal Weight=5-85thpercentile and Underweight ≤ 5th percentile [21].

The laboratory tests included data concerning the following:

- Study of some variables of the glucose homeostasis: Fasting glucose (FG), Fastinginsulin (FI) and oral glucose tolerance test (OGTT) in non-diabetes cases. FG levels were processed with a Vitros 950 lab analyzer, and FI levels with a IMMULITE 1000 analyzer. OGTT was performed after a 12 h fasting period in order to measure glycemia levels at 1, 2 and 3 h after ingestion of 1.75 g/kg body weight powder glucose diluted in 200 mL water (up to maximum 75 g).

In order to assess the insulin-resistance, the Homeostasis model assessment-insulin resistance (HOMA-IR) has been studied, using a accepted calculation formula: FI(μUI/mL) xFG(mmol/L)/22.5 [22].

- Lipid profile: Total Cholesterol (Chol-T) with its fraction high density cholesterol (HDL-C) and Triglycerides (TG). Low density cholesterol(LDL-C) has been calculated with the Friedewald formulae: {LDL-C}={Chol-T}-{HDL-C}-{TG}/5[23].

According to international interpretation grids, correlations are necessary for some variables and for the target age group. The analysis of biochemical changes implies special conditions for blood drawing for certain variables (glycaemia, insulin, hormones), with interpretations depending on age and other technical imposed parameters.

In order to effectively determine the blood type, certain serum-test of O-I, A-II, B-III types are used. One drop of the serum obtained from a patient is mixed with a glass rod with every drop of standard serum. The results are assessed depending on the agglutination reactions for 5 minutes.

The statistic correlation between these samples was appreciated with the p-value Pearson index, considered as being significant for values under 0,05. For statistical analysis, we used the Data-Analysis package and Analysis Toolpakfrom Microsoft Excel 2010 programme (ANOVA; t-student test) and the statistic programme Minitab 19.

Results and discussions

1.The study of ABO blood types rate of occurrence

Statistics have shown that the PCOS sample group includes a higher percent of adolescents with blood type B than the other sample group, the percent being higher than the mean percentage in Romania or even in the world.

If the control sample respects approximately the same rate as the general population in Romania, in the PCOS sample we have a higher rate of B blood type girls (*n=29*) than that of the world for B type group (24%), which is 5% higher than the mean rate for the Romanian population (19%) and with 14% than the rate for the whole world population. For O (*n=39*) and A (*n=48*)blood types,the rate is smaller with 3%, respectively 4% as compared to the control group, while it is only with 2% smaller than the mean rate in our country. As for the AB blood type (*n=6*), there are no significant differences between the PCOS adolescents group and the control sample or the Romania average (table 1).

Table 1

THE STUDY OF ABO BLOOD TYPES RATE OF OCCURRENCE

Blood type groupe	O %	A%	B%	AB%
PCOS girls (n=122)	32	39	24	5
Healthy sample (n=102)	35	43	18	4
Romanian frequency	34	41	19	6
World frequency	46	40	10	4

2.The study of the correlation between ABO/PCOS groups and menstrual abnormalities

The physiological menstrual cycle is determined by the interconnection between the hypothalamic–pituitary–gonadal (HPG) axis. The expression of the symptoms in PCOS adolescents depends on the degree of maturation of the HPG axis which starts at puberty and it is manifested by androgens hypersecretion due to pituitary LH hypersecretion [24].Amenorrhoea, oligomenorrhoea and irregular bleeding were labelled as menstrual disorders maintained after two years of menarche.

In our study AB group blood type includes the cases with the east cycles a year (100%), followed by B blood type sample (93%), while O blood type group has the lowest rate (76.9%) (table 2).

Table 2
THE FREQUENCY OF THE STUDIED FAT TISSUE DISTRIBUTION IN ABO/PCOS BLOOD TYPES GROUPS AND No.OF PERIODS

BMI /Blood type	O %	A %	B %	AB %
Obese	2.0	**23.0**	20.7	13.0
Overweight	41.0	31.0	**48.3**	16.7
Normoponderal	**39.0**	20.8	17.2	**33.3**
Underweight	18.0	**25.0**	13.8	16.7
WC/HC ≥0,8	69.2	64.6	**75.9**	33.3
Period<8/year	76.9	87.5	**93.1**	**100.0**

3. The study of obesity distribution in ABO/PCOS blood types groups

There are a lot of studies showing the positive connection between PCOS and obesity, especially the abdominal obesity, mentioned as occurring in 40% of the PCOS cases [25]and associated with more important metabolic abnormalities in adolescence [26]. It is still not clear if obesity is one of the causes of PCOS or one of its results, but it seems that the latter is more probable [27].WC and the WC/HC report are used as a measure of the visceral adiposity correlated to the risk of occurrence of other serious health problems [28]. The obtained WC and HC values were interpreted according to the international tables which correlate the percentiles for girls depending on age [29]. For children, the high WC values (higher than BMI) have been correlated to the dyslipidaemias and high blood pressure in more than half of the patients with their weight over the cut-off value [30] and with insulin-resistance [31].

Our study on the correlation of the blood type rate with obesity in PCOS teenagers shows the highest percentage for. A blood type (23%), folowed by B blood group (20.7%) and the lowest one for O blood type (2%). There were more overweight cases in B sample group (48.3%) and the lowest rate was in blood type AB (16.7 %).

We may conclude that there were more raised values of the BMI in A and B blood types, with a preferrential abdominal distribution of fat in B blood type. O and AB groups were protective towards the BMI increasing. The WC/HC ratio was the smallest one in AB blood type group (17%), and the highest ratios in B group (76%) (table 2).

4. The study of the glucose homeostasis in ABO/PCOS blood type groups

We have appreciated the variables in the glucose homeostasis in ABO blood type groups asthey have been stated in the chapter describing the work methods. The normal values of basal glycaemia considered for children are the same as for adults, with a cut-off value of 100mg/dL. The normal FI values specified by the analyser range between 6 and 27 μUI/mL.

The interpretation of the glucose tolerance test has been done on the IDF (International Diabets Federation) and ADA(*American Diabetes Association)* recommendation: an impaired glucose tolerance (IGT) is considered for a glycaemia ranging between 140-200 mg/dL after 2 h from drinking glucose solution. The diabetes mellitus (DM) is considered for any value of the glycaemia over 200 mg/dL [32]. Values within 100 and 126 mg/dL place the person in the group considered as *a jeune* glucose metabolism disorder and is called impaired fasting glucose (IFG). Values of the glycaemia under 100 mg/dL at 3 h after drinking glucose solution are considered normal, the same as for the basal plasma glucose. Post prandial hypoglycaemia has been considered for values of the glycaemia lower than 55 mg/dL.

The biochemical variables with high values represented by FG and those obtained at OGTT after 2 and 3 h have been clearly more frequent in B blood type; the lowest values of these variables have been found in O blood type group. The ANOVA statistical differences between the types of blood groups for FG are insignificant, but for insulin *p-value* is 0.0072 On the other hand, the post prandial hypoglycaemia appreciated through OGTT at 3 h has been presented in a higher frequency in A blood type group (42%) and the lowest one in B blood type group (14%). The insulin resistance, appreciated by HOMA-IR values over 3, had a maximum frequency at B girls blood group and minimum at those of O blood group (*p-value=0.00079*) (table 3).

Table 3
THE FREQUENCY OF THE STUDIED GLUCOSE HOMEOSTASIS IN ABO/PCOS BLOOD TYPE GROUPS

Glucose homeostasis	O%	A%	B%	AB%
Glycemia ↗	0.0	12.5	**41.4**	16.7
OGTT 2↗	2.6	12.5	**51.7**	16.7
OGTT 3↗	2.6	12.5	**44.8**	16.7
OGTT 3↘	30.8	**41.7**	13.8	33.3
Insulin ↗	5.1	16.7	**41.4**	**50.0**
Insulin ↘	38.5	**41.7**	27.6	33.3
HOMA-IR	18.0	19.0	45.0	**50.0**

In conclusion, teenagers with blood type B presented more frequently clinical signs of insulin resistance associated with higher values of the FI and FG and of glycaemia at 2 or 3 h from the glucose lunch; moreover, in this group the frequency of hypoglycaemia at 3 h is the least of all. B blood type group is considered a group with glucose-metabolism disorders, and,with risk of developing diabetes mellitus.

5. The study of the lipid metabolism in blood types ABO/PCOS groups

High level of Col-T and of TG and lower levels of HDL-C [33]have been reported at PCOS persons having a weight over normal [34] with a high risk of evolution to diabetes (DM2) [35].Most studies demonstrate the correlation between lipid growth and decreased blood levels of vitamin D [36], other studies reveal a decreasein vitamin A levelsat people with elevated triglycerides [37].

B blood type group includes cases with high rate of raised values of the Col-T (62%), LDL-C (59%) and of TG (34%).Low values for Col-T and TG were in O group. However, no significal p-results in tests for all cholesterol factions, a statistical ANOVA differences between the types of blood groups for TG is significant, *p-value=0.0021.*

The decrease of HDL-C values has been more frequent in Ablood type group (79%), followed by B blood type (72%) and the fewest cases have been met in blood type O group (64%) (table 4).

In people with blood type B group, the rate of cases with high level of TG and LDL-C fraction has been higher than in the other blood type groups, considered to be a group with high risk of atherosclerosis.

Table 4

THE FREQUENCY OF THE STUDIED LIPID METABOLISM IN BLOOD TYPES ABO/PCOS GROUPS

Lipid metabolism	O %	A %	B%	AB%
HDL-C↘	64.1	**79.2**	72.4	66.7
LDL-C↗	30.8	41.7	**58.6**	33.3
Chol-T↗	30.8	41.7	**62.1**	50.0
TG↗	5.1	22.9	**34.5**	33.3

Table 5

STATISTICAL DIFFERENCES BETWEEN THE STUDIED METABOLIC PCOS PARAMETERS FOR THE ABO BLOOD TYPE GROUPS (TURKEY TEST)

N	Media	Group
B	7 40.39	a
AB	7 26.19	a,b
A	7 25.60	a,b
O	7 16.48	b

Surse	DF	SS	MS	F	P
Factor	3	531.7	177.2	5.86	***0.004***

6. The total correlation of metabolic variables in ABO/PCOS blood type sample groups

Studying the all correlations of the variables included in the metabolic disorders in adolescents with different blood types, we have included the following 7 variables: BMI, WC/HC ratio, FG, glycaemia at 2 h and at 3 h during OGTT, FI and the HOMA-IR score.

Although they are not included in the standard definition criteria of PCOS, hyper-insulinemia and insulin-resistance are highly correlated with the PCOS pathogeny [38] and considered as important risk factors for its evolution. There are studies which demonstrated the linear correlation between BMI and insulinemia [39], but the latest years demonstrated the occurrence of insulin-resistance in normal weight people or in those with low BMI [40]. Other studies demonstrate the interdependence between insulin-resistance and hyperandrogeny, but the exact mechanism of this phenomenon is not yet fully clarified, justifying the interest of the specialists in researching this field [41].

There are significant differences between blood type groups concerning the studied parameters, according to the ANOVA unifactorial test which uses the F decision criterion. The *p value* = 0.004 shows the significance of the statistic F criterion. The method explains the significant differences between the variables which are not marked with the same letter (table 5).

Significant statistic differences between the studied variables for the cases in O blood group,as compared to the B blood group, were noticed. The result is similar with some medical studies which appreciated a higher rate of occurrence of the B blood type people and DM2[42]or heart attack [43], or a protective role of the O blood type for DM2 [44]. It is interesting to evaluate how many of these people also have features to PCOS.

Conclusions

Girls with B blood group had a higher rate in PCOS sample compared to the control group, the mean frequency in Romania and in the world. Summarising the results of this study, we have shown that the PCOS adolescents with B blood type have more important changes in the glucose homeostasis than the people with the other blood type groups. Also, the frequency of the cases with anomalies of the values of atherogenic lipoprotein occurs mainly in B blood type sample group. If these changes are associated to the fact that 69% of these girls have BMI over normal, and the fat tissue distribution given by the WC/HC ratio is mainly abdominal (72%), we appreciate that these adolescents have a high risk of developing diabetes and cardiovascular diseases.

At the other end, there are people with O blood type, who presented the lowest frequency of cases with the weight over normal; the lipoprotein anomalies have shown the least cases of high values of the total cholesterol, LDL-C and TG. Still, 68% of the sample group had low levels of the HDL-C, even if it represented the lowest frequency of all blood type groups. Referring to the glucose homeostasis, a very small number of O-positive cases presented anomalies in glucose metabolism, manifested mainly through low values of insulin (40% of the cases), on the second place, after A blood type group, and hypoglycaemia at 3 h after the ingestion of powder glucose (31% of the cases), the third place within the ABO blood types.

O and AB groups behaved in a protective way as compared with the increasing BMI, and the WC/HC ratio had the lowest values in AB group. The menstrual irregularities occurred mainly in AB group(83%).

Subject to ethnicity, we conclude that the study of PCOS adolescents is useful especially for the people in blood type B group due to the associated risk of developing DM2 or cardiovascular diseases.

Abbreviations in text:

PCOS - Polycystic Ovary Syndrome
ESHRE-ASMR - European Society of Human reproduction and Embriology / American Society of Reproduction Medicine
WC - waist circumference
HC - hip circumference
BMI - body mass index
DM - Diabetes mellitus
DM2 - type 2 diabetes mellitus
FG - Fasting glucose
FI - Fasting insulin
OGTT - Oral glucose tolerance test
HOMA-IR - Homeostasis model assessment - insulin resistance
Col T - Total Cholesterol
HDL-C - High density cholesterol
LDL-C - Low density cholesterol
TG - Triglycerides
IFG - Impaired fasting glucose
IGT - impaired glucose tolerance

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