Volume 10 / Number 3 / 2016 ISSN 1840-2291

HealthMED

Journal of Society for development in new net environment in B&H

Volume 10 / Number 3 / 2016

HealthMED

Journal of Society for development in new net environment in B&H

Address Bolnicka bb, 71 000 Sarajevo,
Bosnia and Herzegovina.
Editorial Board e-mail: healthmedjournal@gmail.com web page: http://www.healthmed.ba
Published by DRUNPP, Sarajevo
Volume 10 Number 3, 2016
ISSN 1840-2291 e-ISSN 1986-8103

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Correlation between Gestational Age and Ultrasound Fetoplacental Parameters in Fetuses withIntrauterine Growth Restriction

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Abstract

Aim: The aim of this study wasto determine the correlationbetween gestational age and ultrasound fetoplacental parametersin fetuses with intrauterine growth restriction (IUGR).

Methods and material: A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR *(n=60)*. Outcome measures were following ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR: Fetal Liver Length (FLL), Femur Length (FL), Biparietal Diameter (BPD), andAmniotic Fluid Index (AFI).Sonography was carried out by sonda3.5 Mhz type MINDRAY DC 7.

Results: There is a significant association between the placental maturation and the diagnosis [$\chi^2(3)= 24.216$; $p < 0.001$]. There was a strong positive correlation between gestational age and following ultrasound fetoplacental parameters: BPD, FL and FLL in fetuses with non and fetuses with IUGR. There was a strong negative correlation between AFI and following parameters: FL, FLL and BDP in fetuses of both groups.There was a strong positive correlation between FLL and following parameters: FL and BDP, than between FL and BDP in non IUGR and IUGR groups.

Conclusion: In a fetus with IUGR there is strong negative corelation between gestational age and AFI and strong positive correlation between gestational age and BPD, FL and FLL.

Key words: intrauterine growth restriction, ultrasound fetoplacental parameters, gestational age

Introduction

A fetus with intrauterine growth restriction (IUGR) is a fetus with an estimated weight less than the 10th percentile for gestational age (1,2). With a prevalence of the 5–8% in the general population, IUGR affects approximately 7–15% of worldwide pregnancies (2,3,4). Clinical assessment alone is not adequate in pregnancies at high risk for IUGR, given the low sensitivity and specificity and ultrasonography should be used to try to confirm or exclude the diagnosis (1). In the USA, and many other countries women are selected for third trimester ultrasonography on the basis of pre-pregnancy risk factors, development of obstetric complications, and serial measurement of symphyseal-fundal height (5). In the study of Vermeer N et al., an isolated short femur is associated with intrauterine growth restriction and adverse pregnancy outcome (6). Dacaj et al. found that fetuses in IUGR group had significantly lower median value of Fetal Liver Length (FLL), Femur Length (FL), Biparietal Diameter (BPD), and Amniotic Fluid Index (AFI) compared to non IUGR group (7). Combined testing by maternal characteristics and fetal biometry at 30-34 weeks [Z-scores of Fetal Head Circumference (HC), Abdominal Circumference (AC) and FL or Estimated Fetal Weight (EFW)]could identify a high proportion of pregnancies that will deliver small for gestational age (SGA) neonates (8). In about 75% of the cases, IUGR remains unrecognized until birth and the diagnosis comes retrospectively, whereas in low-risk pregnancy the detection rate is about 15% (9). The investigation of IUGR has the aim of an early detection and appropriate management that could reduce rates of perinatal morbidity and mortality.

The aim of this study wasto determine the correlationbetween gestational age and ultrasound fetoplacental parameters in fetuses with IUGR.

Materials and Methods

A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR *(n=60)*.The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women. Preeclampsia was determined with method of Last Menstrual Period (LMP), Hadlock's formula on the basis of presence of proteinuria (> 0.5 g/L) and high blood pressure (TA = 140/90 mmHg) (10). Antenatal diagnosis of IUGR was based on sonographic evaluation of the fetus, placenta, and amniotic fluid. Sonography was carried out by sonda3.5 Mhz type MINDRAY DC 7. Outcome measures were following ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR: Fetal Liver Length (FLL), Femur Length (FL), Biparietal Diameter (BPD), and Amniotic Fluid Index (AFI).

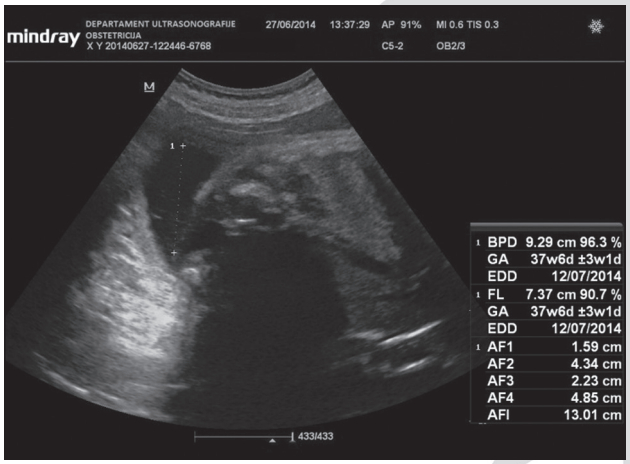

Figure 1. Measurement of AFI.

A pregnant woman lying on her back, the uterus is divided into four equivalent quadrants, so that the umbilicus and the *lineanigra*used as markers. After placing the gel, the ultrasound is placed perpendicularlyand parallel to the spinal column. It is measured the depth of the largest pockets of amniotic fluid, without the presence of the umbilicus and small parts of the fetus (extremities) in four quadrants. AFI represents a numerical sum of all four quadrants expressed in cm.

Results are expressed as mean value and standard deviation in case of normal distributed continue variables**,** as median and interquartile range (IQR) in case of non-normal distributed continue variables. A Spearman's rank-order correlation was run to assess the relationship between gestational age andultrasound fetoplacental parameters. In case of categorical variables, counts and percentages were reported. Categorical data were analyzed with Pearson's Chi-Square test or Fisher's Exact test. A p-value <0.05 was considered as significant. Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS Release 19.0; SPSS Inc., Chicago, Illinois, United States of America) software.

Results

There is a significant association between the placental maturation and the diagnosis [$\chi^2(3)$= 24.216; $p < 0.001$]. The most ofwomen with preeclampsia and IUGR had grade III of placental maturation (48.3%). *(Table 1).*

Table 1. Characteristics of pregnant womanin both groups

Variables	IUGR (n=60)	non IUGR (n=60)	p-value
Week of gestation	37 (32 to 38)	38 (36 to 39)	0.068
Stage of placental maturation (%)			
0	3.3	13.3	<0.001
I	16.7	38.3	
II	31.7	38.3	
III	48.3	10.1	

There was a positive correlation between gestational age and BPD in fetuses with non IUGR (r_s = *.983,p< .001)* and fetuses with IUGR (r_s = *1.00,p< .001)(Figure 1).*There was a negative correlation between gestational age and AFI in fetuses with non IUGR *(r_s = - .853; p <.001)* and fetuses with IUGR*(r_s = - .904; p < .001).(Figure 2).*

There was a positive correlation between gestational age and FL in fetuses with non IUGR *(r_s = .992; p <.001)* and fetuses with IUGR*(r_s = .999; p < .001). (Figure 3).*

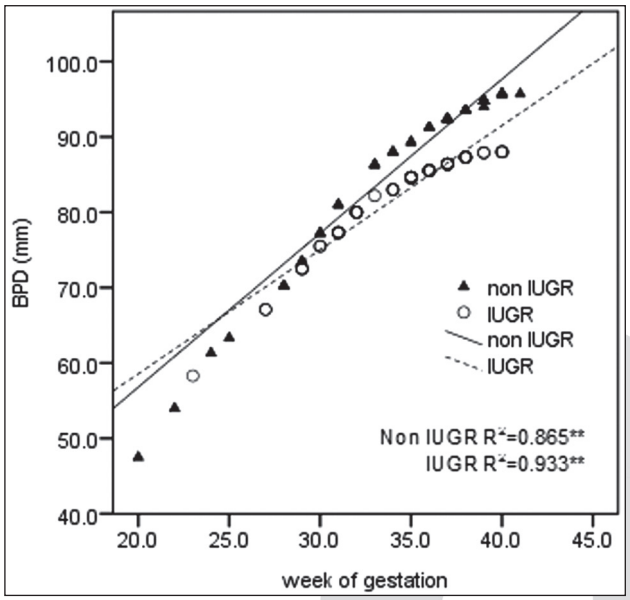

*Figure 2. Correlation between gestational age and Biparietal Diameter (BPD) in non IUGR and IUGR groups(R^2 = coefficient of determination, ** p < .001)*

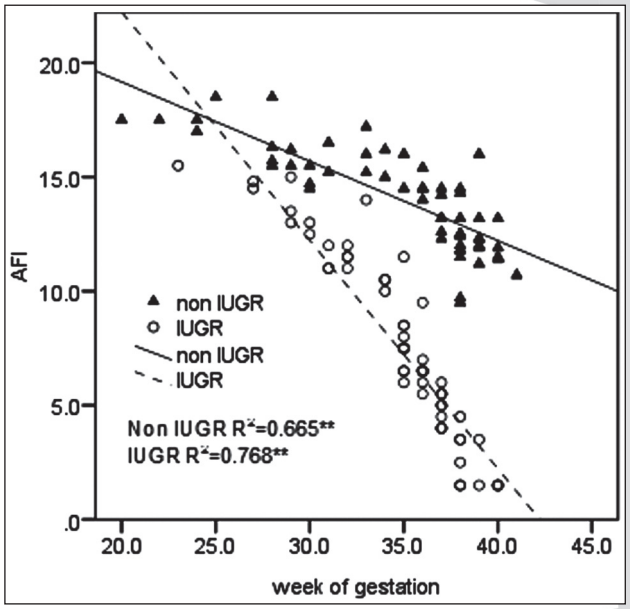

*Figure 3. Correlation between gestational age and Amniotic Fluid Index (AFI)in non IUGR and IUGR groups (R^2 = coefficient of determination, ** p < .001)*

There was a positive correlation between gestational age and FLL in fetuses with non IUGR *(r_s= 1.00; p <.001)* and fetuses with IUGR*(r_s= .997; p < .001).(Figure 4).*

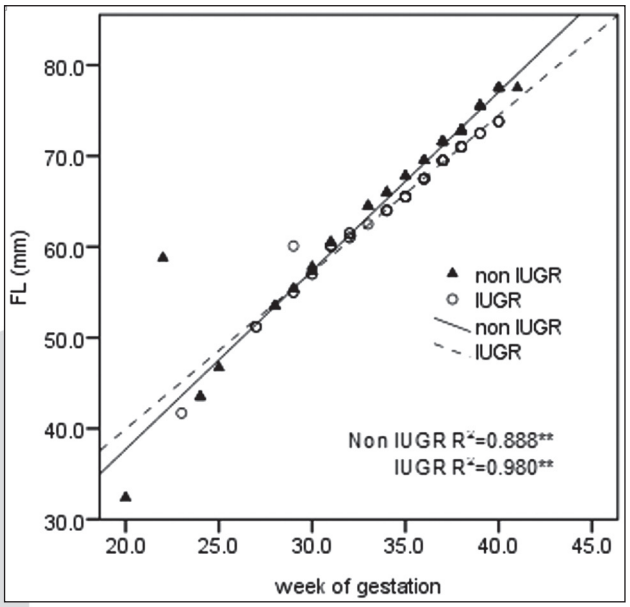

*Figure 4. Correlation between gestational age and Femur Length (FL) in non IUGR and IUGR groups (R^2 = coefficient of determination, ** p< .001)*

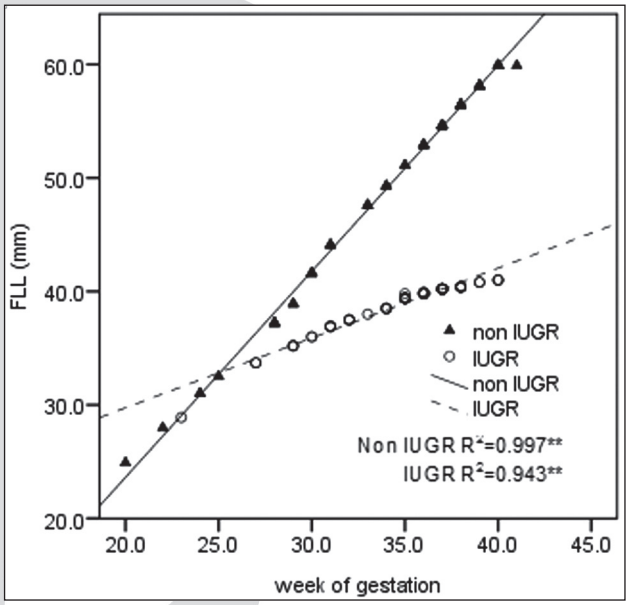

*Figure 5. Correlation between gestational age and Fetal Liver Length (FLL) in non IUGR and IUGR groups (R^2 = coefficient of determination, ** p < .001)*

In fetuses with non IUGR, there was: a negative correlation between AFI and FLL *(r_s= - .852; p < .001),FL (r_s= - .837; p < .001)* and BDP *(r_s= - .845; p < .001);* a positive correlation between FLL and FL *(r_s= .992; p < .001)* and BDP *(r_s= .983; p < .001);* a positive correlation between FL and BDP *(r_s= .977; p < .001).*In fetuses with IUGR, there was: a negative correlation between AFI and FLL

(r_s= - .904; p < .001),FL (r_s= - .902; p < .001) and BDP *(r_s= - .904; p < .001);* a positive correlation between FLL and FL *(r_s= .999; p < .001)* and BDP *(r_s= 1.00; p < .001);*a positive correlation between FL and BDP *(r_s= .999; p < .001).*

In fetuses with non IUGR, there were: a negative correlation between fetal weight and AFI (r_s=-.760; p<.001); a positive correlation between fetal weight and: FLL (r_s=.872; p<.001), FL (r_s=.866; p<.001) and BDP (r_s=.863; p<0.001). In fetuses with IUGR, there were: a negative correlation between fetal weight and AFI (r_s=-.700; p<.001); a positive correlation between fetal weight and: FLL (r_s=.792; p<.001), FL (r_s=.793; p<.001) and BDP (r_s=.793; p<0.001).

Discussion

In this prospective study, we evaluated ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR and we calculated the correlation betwen gestational age and these parameters. In our study, there was a strong positive correlation between gestational age and following ultrasound fetoplacental parameters: BPD, FL and FLL in fetuses with non IUGR and fetuses with IUGR and there is a strong negative correlation between gestational age andAFI in both groups. Fetuses in IUGR group had lower median value of AFI (Me = 6.5 cm, IQR = 4.5 to 11.0) compared to non IUGR group (Me = 14.3 cm, IQR = 12.3 to 15.7), p < .001. In a large retrospective study conducted by Petrozella et al,a borderlineAFI (defined as 5–8 cm) diagnosed between 24 and 34weeks' gestation, when compared to pregnancies with anormal AFI (8–24 cm), was associated with higher rates ofmajor fetal malformations and in the absence of malformations was associated with an increased risk of IUGR,preterm birth (both spontaneous and iatrogenic), andcesarean delivery for fetal intolerance of labor (11). In retrospective cohort study of Wood SL et al., pregnancies with a borderline AFI had a relative risk of 13.76 for concurrent IUGR (p < .001) (12). Gumus et al., reported an increased incidence of IUGR in pregnancies with a borderline AFI. They suggested careful monitoring in the setting of an AFI between 5 and 10 cm (13).There is a direct relationship between decreased amniotic fluid volume and the prevalence of IUGR. When a single pocket of amniotic fluid is >2cm, between 1 and 2 cm and <1 cm, the prevalence of IUGR is 5%, 20% and 37%, respectively (14). In our study, there was a strong negative correlation between AFI and following parameters: FL, FLL and BDP in fetuses of both groups.There was a strong positive correlation between FLL and following parameters: FL and BDP, than between FL and BDP in non IUGR and IUGR groups.

Conclusion

In a fetus with IUGR in preeclampsia there is strong negative corelation between gestational age and AFI and strong positive correlation between gestational age and BPD, FL and FLL.

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The Acute Effects of Short-term Insulin Therapy on the Secretory Ability of Beta Cells in Patients with Diabetes Mellitus Type 2, After the Secondary Failure of the Oral Therapy

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Abstract

Introduction: Secondary failure (SF) to treatment with oral therapy is defined as the absence of a favorable reaction to the oral therapy which was effective in the previous course of the treatment. The aim of the work was to investigate the acute effects of the short-term insulin therapy on the secretory ability of endocrine pancreatic beta cells and the insulin resistance.

Materials and Methods: 98 patients with diabetes mellitus type 2 (DM T2) and confirmed the SF to the oral therapy were selected for the study. These patients were divided into two different groups based on their body weight, and each group received a different insulin treatment regimens. The patients with a normal body mass (group A) were treated with a mono-insulin intensive conventional therapy (so called Basal-bolus regimen), while the group B patients (the group with an increased body mass) were treated with a combined insulin therapy (basal insulin plus metformin) in the duration of three months. All involved patients were tested prior to the insulin therapy and then three months after its startfor the factors of glycoregulation (glycated hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), 2h postprandial glucose (2h-PPG) and self-monitoring of blood glucose (SMBG), and the homeostatic models for the estimation of values forthe insulin secretion and resistance (HOMA-β% and HOMA-IR) were calculated from the pairs of fasting glycemia and insulinemia.

Main results: Results of the study show the improvement in glycoregulation, a decrease in insulin resistance (IR) and improvement in the endogenous pancreatic capacity for the both tested groups, when compared to the period prior to the insulin therapy started. Group A: FPG (9.5 vs. 6.1,p<0.001), 2h-PPG (11.6 vs. 6.9, p<0.001), HbA1c (9.0 vs. 6.7, p<0,001), HOMA-β % (39.03 vs. 83.42, p<0.001), HOMA-IR(4.87 vs. 2.45, p<0.001). Group B: FPG (9.4 vs. 6.3, p<0.001), 2h-PPG (11.6 vs. 6.9, p<0.001), HbA1c (9.0 vs. 6.7, p<0.001), HOMA-β% (54.8 vs. 96.92, p<0.001), HOMA-IR (7.27 vs. 3.38, p<0.001).

Conclusion: The short-term insulin therapy, including normal-weight and overweight patients with DM T2 results in an improvement of glycoregulation, decrease in insulin resistance and recovery of secretory ability of beta cells of endocrine pancreas.

Key words: secondary failure, diabetes mellitus type 2, HOMA-β%, HOMA-IR.

Introduction

Secondary failure (SF) to treatment with oral therapy is defined as an absence of the favorable reaction to the oral therapy which was efficacious in the previous course of the disease (1). Although the SF pathogenesis is not completely understood, the effects of glycotoxic impacts to the occurrence of SF to oral therapy isundoubtable (2,3). The very moment of appearance of the secondary therapeutic failure in patients with diabetes mellitus type 2, if it is not conjoined with the evidently present criterions for the usage of insulin therapy, represents the critical point in the therapy dilemma (4). Introduction of insulin, by either the regimen of the combined or the monoinsulin therapy is a chief and most frequent used therapeutic procedure (5,6). The dilemma is

pertaining the patients in which there no clear clinical and biochemical evidence of significant insulin deficiency. Because of this, there is an increase of interest in the introduction of short-term insulin therapy with the main goal to counteract glucose toxicity in these patients. Edmond et al. mentioned in their study that the short-terminsulin therapy in duration of only 2-3 weeks achieved a euglycemia in 90% of the patients, with improvement in beta-cell function and a decrease in insulinresistance (7). The similar results mentioned Chen et al. who evaluated the effects of the short-terminsulin therapy on beta-cell function and insulin sensitivity, showing a significant improvement in the tested parameters and also keeping up the long-term effects of the short-terminsulin therapy in the glycemic control in the post-insulin administration period (8). The partial reversibility of the basic defects in excretion and effect of insulin, in the state of corrected glycemia, represents the main pathophysiological base in implementation of short-term insulin therapy in patients with DM T2 and shown SF to oral therapy.

Likewise, the goal of the study represents the investigation on acute effects of the short-terminsulin therapy to the secretory ability of beta cells in endocrine pancreas and insulinresistance.

Materials and Methods

The prospective study was conducted in the Clinic for Endocrinology, Diabetes and Metabolism Diseases and in the Clinical Center of Banja Luka-Endocrinology Day Hospital, from September 2010 to May 2014. The study included 98 patients suffering from DM T2 and with a confirmed SF to oral therapy, age group between 48-60. The criterions for study inclusion were as following: FPG value greater than 7 mmol/L, 2h-PPG value above 9 mmol/L, and HbA1c above 7,5%, in accordance with the National Guidelines for Good Clinical Practice (9). The study did not include elderly patients with an impaired liver or kidney function, the patients with other endocrine or infective diseases, the patients on therapy with corticosteroids one month prior to the beginning of the study, and the patients with an exceptionally low glycoregulation values (HbA1c >10%). Nine of the tested patients developed heart insufficiency, four developed a malignant disease, while eight of the tested patients were „lost“ in the course of study, so that the study was finished with 77 tested patients, in total. All involved patients were tested prior to the insulin therapy and then three months after its start for the degree of glycoregulationby morning glycemic values, postprandial glycemia, daily glycemia values and glycolysed hemoglobin (HbA1c), while the insulin-secretory function was estimated based on the homeostatic models for estimation of insulin secretion (HOMA-β % and HOMA-IR). The protocol of the study was approved by the Ethical Committee. All patients signed their written approval for participation in the study. Biochemical blood analyses for the lab testing were done in the morning, after 12-hour of overnight fasting, for the following parameters: HbA1C, fasting glycemic value and insulin. Body mass index (BMI) calculation was done by the Quetelet's formula: BMI= body mass in kg/square meter of body height (kg/m^2). Glycemia was determined by the hexokinase method, with the referent values for the method of 4.1-5.9 mmol/L. Insulin was determined by the ECLIA method (electrochemilluminescence) on the COBAS E411 machine, by Roche, with referent values of 2.6-24.9 mU/ml. Insulinresistance (IR) is a state when normal insulin levels cannot achieve a biological response. Homeostatic model for IR (HOMA-IR) was determined from the pairing of insulin values and fasting glycemic value, according to the following formula: HOMA-IR=Glucose x Insulin/22.5, with referent values of up to 2.5. This model correlates very well with the euglycemic clamp (r=0.88) (10,11). The secretory capacity of beta-cells is expressed via the homeostatic model for estimation of insulin secretion (HOMA-β %), which was determined mathematically from the insulin and fasting glycemic value pairs, according to the following formula: HOMA-β = 20 x FastingInsulin / Fasting glycemia - 3.5 ٪. The values of this parameter depend on HOMA-IR and its normal value is about 100%. With the intent of creating homogenous tested groups and based on the fact on the SF of oral therapy, all the patients were divided into two groups: 1. Patients with the normal body mass (BMI ≤ 25kg/m^2), group A. 2. Patients with increased body mass (BMI ≥ 26kg/m^2), group B. Each group was treated with a different insulin regimen and the obtained data were analyzed separately. Group A (n=34) was on an intensive insulin therapy (so-called Basal-bolus regimen). A

starting dose of the prandial insulin (aspart, glulisin or lispro) was 5U before the meal and 10-15 units of basal insulin (detemir, glargin) within 22 hours, with dose adjustment during the follow-up. Group B (n=33) was treated with a combined insulin therapy: starting dose of 10 units of basal insulin (glargin, detemir) within 22 hours, with dose adjustment during the follow-up, and 2000 mg of metformin, divided in two daily doses.

Statistics

Data analysis end extrapolation were done by the methods of descriptive statistics. The Student's t-test for independent samples, were used for comparison of differences between the groups. The threshold of significance was a probability of $p<0.05$. The statistics, graphs, and tables of the results were done in MS Office Word 2007, MS Office Excel 2007, and SPSS 16.0 for Windows.

Results

The two tested groups did not have significant difference in gender, known length of the disease until the time of SF occurrence, FPG, 2h-PPG and HbA1c. Apart from the BMI, the two groups differed in age, with the average age was somewhat greater in group A, with the average difference of 2.3 years ($t=2.576$; $p=0.012$). (Table 1).

Glycoregulation

Table 2. shows the parameters of glycoregulation of both tested groups, before and after the insulin treatment. Looking in general, there is a statistically significant decrease of all observed parameters of glycoregulation for the both tested groups ($p<0.001$) after the short-term insulin treatment. However, there is not so great a difference in the time period after insulin therapy for the postprandial glycemia, which means there is a statistically significant influence between the type of therapy on the difference of this parameter ($F=9.026$; $p<0.001$).

Table 1. Basal characteristics of the tested patients

Variable	Group A		Group B	
Sex	Male	Female	Male	Female
	18	16	16	17
Age (years)	57.1 ±1.0		54.8±4.8*	
Duration of diabetes (years)	7.8±2.1		7.3±2.0	
Body mass index-BMI (kg/m2)	22.9±1.2		28.1±1.1	
Fasting plasma glucose – FPG (mmol/l)	9.5±0.8		9.4±0.9	
2h postprandial glucose - 2h-PPG (mmol/l)	11.6±1.5		11.3±1.9	
Glycated hemoglobin A1c - HbA1c (%)	9.0±0.6		8.9±0.5	

*Note: Values are the mean ± SD. *p<0.05 for Group A age before vs Group B age.*

Table 2. Glycoregulation before and after three months of insulin therapy

Variable		Group A n=34	Group B n=33
Fasting plasma glucose – FPG (mmol/l)	Before	9.5 ± 0.8	9.4±0.9
	After	6.1±0.2	6,3±0.4
	t-test	p<0.001	p<0.001
2h postprandial glucose – 2h-PPG (mmol/l)	Before	11.6±1.5	11.3±1.9
	After	6.9±0.5	7.3±0.4
	t-test	p<0.001	p<0.001
Self-monitoring of blood glucose - SMBG (mmol/l)	Before	10.3±1.3	9.6±0.9
	After	7.3±0.3	7.2±0.3
	t-test	p<0.001	p<0.001
Glycated hemoglobin A1c - HbA1c (%)	Before	9.0±0.6	8.9±0.5
	After	6.7±0.3	6.8±0.2
	t-test	p<0.001	p<0.001

Note: Values are the mean ± SD, p<0.05 for Group A before vs. After, p<0.05 for Group B before vs. After. Paired Samples. t-test.);

HOMA-β % and HOMA-IR

Average value HOMA-β % in the group with normal BMI before insulin therapy was 39.3±٧,19, while after three months of the treatment a statistically significant increase was marked in the value for this parameter to 83.42±8.41, p<0.001. The normal BMI group showed an improved response in beta-cell secretory capacity, when compared to beginning of the study (54.8±8.55 vs. 96.92±12.91, p<0.001) (Table 3). The group with normal body mass had the average value of HOMA-IR 4.87±0.66 before insulin therapy, while after the therapy there is a statistically significant decrease in this parameter, with the value 2.45±0.24 (p<0.001). This points out to the existence of a significant degree of insulin resistance in the tested patients, as an important factor for appearance of secondary therapeutic failure.

The group of overweight patients also showed a decrease of IR after the three-month therapy, estimated by HOMA-IR (7.27±1.99 vs. 3.38 ±0.78, p<0.001). The average value of HOMA- IR as a homeostatic model for estimation of insulin resistance was 7.27±1.99 prior to the therapy, and 3.38±0.78 after the three-month therapy (Table 3).

Table 3. HOMA-β % and HOMA IR- Before and after of insulin therapy

Variable		Group A n=34	Group B n=33
HOMA-β (%)	Before	39.03±2.19	54.8±8.55
	After	83.42±8.41	96.92±12.91
	t-test	p<0.001	p<0.001
HOMA-IR	Before	4.87±0.66	7.27±1.99
	After	2.45±0.24	3.38±0.78
	t-test	p<0001	p<0.001

Note: Values are the mean ± SD, p<0.05 for Group A before vs. After, p<0.05 for Group B before vs. After. Paired Samples.t-test.); HOMA-β % homeostatic model assessment of insulin secretion; HOMA-IR homeostatic model assessment of insulin resistance.

Discussion

The results of our study show that the effects of three-month insulin therapy on all parameters of glycoregulation were satisfactory and had similar values in both tested groups. The fact that there were no significant differences in levels of glycoregulation between the groups, meaning that the both therapeutic regimens had the same effects, is an important one. The investigations indicate that the glycemic normalization achieved by any therapeutic choice can lead to the recovery of beta cell function and decrease in the degree of resistance to insulin, which was also shown in our study (12,13). Far backin 1984, Andrews WJ et al. shown the results of test on 13 overweight patients with the type two diabetes who experienced an improvement in insulin secretion (up to 2.5 times) and in insulin effect (14) after the intensive insulin therapy for one month. Campos, in his study, emphasized the negative effects of the chronic exposure of beta-cells to the high concentrations of glucose which in turn impaired the insulin response and increased resistance to insulin effects (15). Hence, hyperglycemia, when observed as not only a consequence but also as a cause of destabilization of metabolic state in diabetes, represent a necessity for therapy intervention, with the aim of breaking the positive-feedback circle in which a hyperglycemia bears the new and even higher hyperglycemia (16,17). The insulin therapy of our study lasted for three months. This period of time was chosen based on the previously published results of the studies which tested efficacy of different time periods for insulintreatment of patients with diabetes type 2. Previous *in vitro* studies showed that only 20 hours of normolgycemia caused the partial recovery of insulin-secretory function. Testing insulin-secretory function just prior to introduction of insulin therapy showed that all tested patients exhibited the signs of basal hyperinsulinemia. The group of patients with increased body mass showed the higher values for the basal insulinemia, compared to the group of patients with a normal body mass. Such a finding of increased values of basal insulinemia, in the environment of high glycemia, is a consequence of either resistance to insulin or increased concentration of biologically less active insulin precursors. After the three-month insulin therapy, both tested groups exhibited decrease in the values of basal insulinemia. Another possible explanation for the lowered basal insulinemia may lay in the possibility of lowering the level of insulin precursors (proinsulin and its products) after the metabolic stabilization, which was mentioned in literature. The results of our study show that the homeostatic model for the estimation of residual of beta cell function (HOMA-β%) considerably lower in the non-overweight group of patients, which

points out to the fact that the overweight patients had a better insulin-secretory function, on the average. A number of studies showed that HOMA-β% index for estimation of residual of beta cell function in the secondary therapeutic failure is a quite good indicator of insulin dependence. Other studies did not completely corroborate with this finding with an emphasis on a possibility of partial recovery of beta-cell function by removal of glucose toxicity, which was confirmed in our study. Kadhem et al. investigated the connection between the glycolysed hemoglobin (HbA1c) and HOMA index in diabetes type 2 and emphasized that HbA1c is a good predictor of beta-cell function, which was confirmed by our study (18). Although the both therapeutic regimens were equally efficacious in sense of glycoregulation, the therapy with both insulin and metformin had a better efficacy in lowering insulin resistance, when a considerable degree of insulin resistance in the overweight group is taken in consideration. Since it is known that the level of achieved glycoregulation was very similar, then the improvement of the insulin response has to be attributed to the effect of metformin and not exclusively to the removal of glucose toxicity. It is important to emphasize that even though the insulin resistance was there, there was a sufficient glycoregulation after the insulin introduction, suggesting that the insulin resistance is not a dominant factor for the non-regulated glycemia, but there are existing some other factors that are imposing glycoregulation.

Conclusion

Our results show that short-term insulin therapy in normal and overweight patients with diabetes type 2 improves glycoregulation and leads to a partial recovery of secretion of insulin and lowering the level of its resistance. The overweight patients showed the signs of a lower degree in insulin secretory deficiency and a greater degree of insulin resistance, compared to the other group. The intermittent, short-term insulin therapy, as a monotherapy or a combined therapy is a rational alternative to the long-term insulin therapy in well-selected patients.

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Ratio of Fetal Liver Length and Level of Aminotransferases in Serum of Fetuses with Intrauterine Growth Restriction

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Abstract

Aim: The aim of this study wasto compare the ratio of fetal liver length (FLL) and level of aminotransferasesin fetuses with intrauterine growth restriction (IUGR).

Methods and material: A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR *(n=60)*.Outcome measures were followingvariables: aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin (indirect and direct) and fetal liver length (FLL). A bloodfor analysis was drawn from the umbilical vein of the fetuses during delivery period. Sonography was carried out by sonda3.5 Mhz type MINDRAY DC 7.

Results: The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women, p > 0.05. There was a significant a negative correlation between gestational age and levels of indirect bilirubin (r_s = .666,p< .001)and direct bilirubin(r_s = .673,p<.001in serum of fetuses with IUGR. Median FLL / AST ratio was statistically significantly lower in IUGR (1.7) compared withnon IUGR fetuses (2.1), U = 1 084, z = -3.758, p< .001 Median FLL / ALT ratio was statistically significantly lower in IUGR (3.1) compared with non IUGR fetuses(4.7), U = 655.5, z = -6.007, p< .001.

Conclusion: Ratio of FLL / AST and ratio of FLL / ALT weresignificantly lower in IUGR compared with non IUGR fetuses. In a fetus with IUGR there was negative correlation between gestational age and levels of indirect and direct bilirubin.

Key words: intrauterine growth restriction, fetal liver length, aminotransferases, gestational age

Introduction

Intrauterine growth restriction (IUGR) represents the second cause of perinatal mortality, after prematurity, and it is related to an increased risk of perinatal complication (1). The fetal liver is indubitably the earliest and most markedly affected organ by abnormal fetal growth and liver perfusion is reduced to 30% (2,3). Normal fetal liver length has a linear relation to gestational age, and showed a significantly rapid increase after 28th week with a growth rate of 1.76 mm per week, and 1.00 mm per week before 28th week (4). In the study of Liu Z et al., the growth rate of IUGR group before and after therapy were 1.19 mm and 1.23 mm per week, significantly lower than those of normal group (p< 0.05).In the study of Kuno A et al., authors suggested that liver volume may be a useful measurement for diagnosing small for gestational age (SGA) fetuses in the mid to late third trimester but that liver length may not be predictive (5).Dacaj et al. found that fetuses in IUGR group had significantly lower median value of Fetal Liver Length (FLL) and aminotransferases in serum, compared to non IUGR group (6,7).Clinical assessment alone is not adequate in pregnancies at high risk for IUGR, given the low sensitivity and specificity and ultrasonography should be used to try to confirm or exclude the diagnosis (8). In the literature we find hepatic morphometric parameters in the human fetus (9,10), but we failed to find complete information about of ratio of morphometric parameters of fetal liver and levels of transaminases in serum of fetuses with IUGR. The investigation of IUGR has the aim of an early detection and appropriate management that could reduce rates of perinatal morbidity and mortality. The aim of this study wasto compare the ratio of fetal liver length (FLL) and level of aminotransferases in fetuses with intrauterine growth restriction (IUGR).

Materials and Methods

A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR *(n=60)*.Preeclampsia was determined with method of Last Menstrual Period (LMP), Hadlock's formula on the basis of presence of proteinuria (> 0.5 g/L) and high blood pressure (TA = 140/90 mmHg) (11). Antenatal diagnosis of IUGR was based on sonographic evaluation of the fetus, placenta, and amniotic fluid. Outcome measures were followingvariables: aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin (indirect and direct) and fetal liver length (FLL). A bloodfor analysis was drawn from the umbilical vein of the fetuses during delivery period. Sonography was carried out by sonda 3.5 Mhz type MINDRAY DC 7. Results are expressed as mean value and standard deviation in case of normal distributed continue variables, as median and interquartile range (IQR) in case of non-normal distributed continue variables. In case of categorical variables, counts and percentages were reported. Categorical data were analyzed with Pearson's Chi-Square test or Fisher's Exact test. Statistical analysis comparing the two groups was performed with Independent Sample T-test for continuous normal distributed variables and Mann–Whitney *U*-test for continuous non-normal distributed variables. A Spearman's rank-order correlation was run to assess the relationship between gestational age andlevels of direct and indirect bilirubin in serum of fetuses. A p-value <0.05 was considered as significant. Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS Release 19.0; SPSS Inc., Chicago, Illinois,United States of America) software.

Results

The mean of maternal age was 30.0±6.1 years in group with preeclampsia and IUGR and 28.1±5.1 years in non IUGR group*(p* > 0.05*)*.There is a significant association between the placental maturation and IUGR [$\chi^2(3)$= 24 216; $p < 0.001$].The most ofwomen with preeclampsia and IUGR had grade III of placental maturation (48.3%).

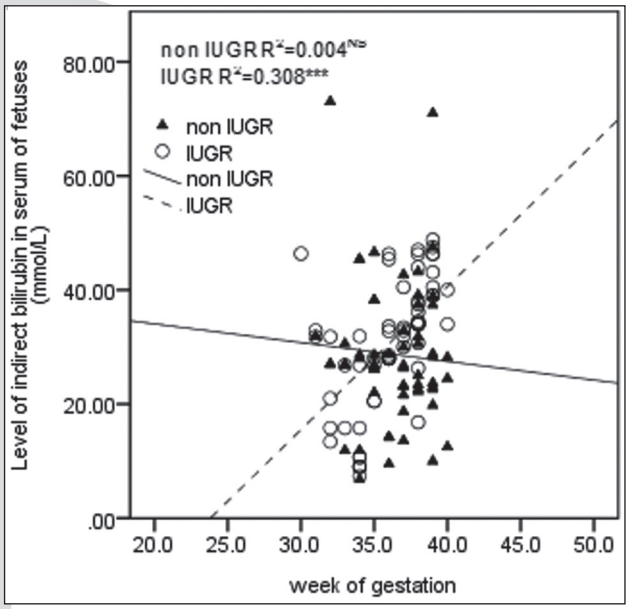

Figure 1. Correlation between gestational age and level of indirect bilirubin in serum of fetuses (mmol/L)in non IUGR and IUGR groups
*(R^2 = coefficient of determination, ***p< .001, NS = non significant)*

Table 1. Variables in fetuses with non IUGR and IUGR

Variables	IUGR (n=60)	non IUGR (n=60)	p-value
AST (U/L)	24.0 (21.0 to 31.0)	22.5 (12.3 to 30.1)	0.014
ALT (U/L)	14.0 (12.0 to 18.0)	10.0 (9.0 to 13.0)	<0.001
Indirect bilirubin (mmol/L)	32.4 (26.4 to 39.0)	27.0 (22.6 to 32.6)	0.054
Direct bilirubin (mmol/L)	16.6 (6.8 to 23.1)	10.4 (6.9 to 13.3)	0.042
FLL (mm)	42.0 (40.9 to 42.7)	54.6 (44.1 to 56.4)	<0.001
Ratio of FLL / AST	1.7 (1.2 to 2.0)	2.1 (1.6 to 4.2)	<0.001
Ratio of FLL / ALT	3.1 (2.3 to 3.6)	4.7 (3.9 to 6.2)	<0.001

Note: Continuous variables are expressed as median with interquartile range (IQR, 25th to 75th percentiles), statistics by Mann-Whitney. Definition of abbreviations, IUGR = Intrauterine growth restriction; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; LDH = Lactate dehydrogenase; FLL = Fetal liver length;

There was not a significant a negative correlation between gestational age and level of indirect bilirubin in serum of fetuses with non IUGR (r_s = - .063,p> .05*)*. There was a significant a negative correlation between gestational age and level of indirect bilirubin in serum of fetuses with IUGR (r_s = .666,p< .001) *(Figure 1)*.

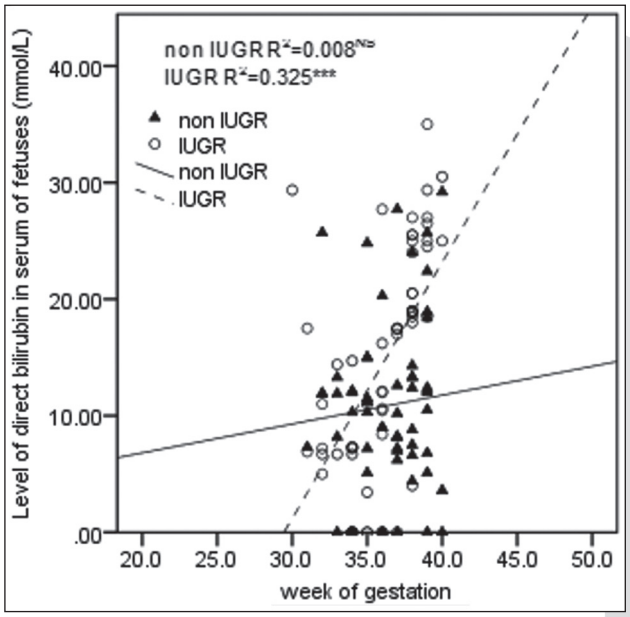

Figure 2. Correlation between gestational age and level of direct bilirubin in serum of fetuses (mmol/L) in non IUGR and IUGR groups
*(R^2 = coefficient of determination, ***p< .001, NS = non significant)*

There was not a significant a negative correlation between gestational age and level of direct bilirubin in serum of fetuses with non IUGR (r_s = - .060, p> .05*)*. There was a significant a negative correlation between gestational age and level of direct bilirubin in serum of fetuses with IUGR (r_s = .673,p<.001*) (Figure 2)*.

Median FLL / AST ratio was statistically significantly lower in IUGR (1.7) compared with non IUGR (2.1), U = 1 084, z = -3.758, p< .001 *(Figure 3)*. Median FLL / ALT ratio was statistically significantly lower in IUGR (3.1) compared with non IUGR (4.7), U = 655.5, z = -6.007, p< .001 *(Figure 4)*.

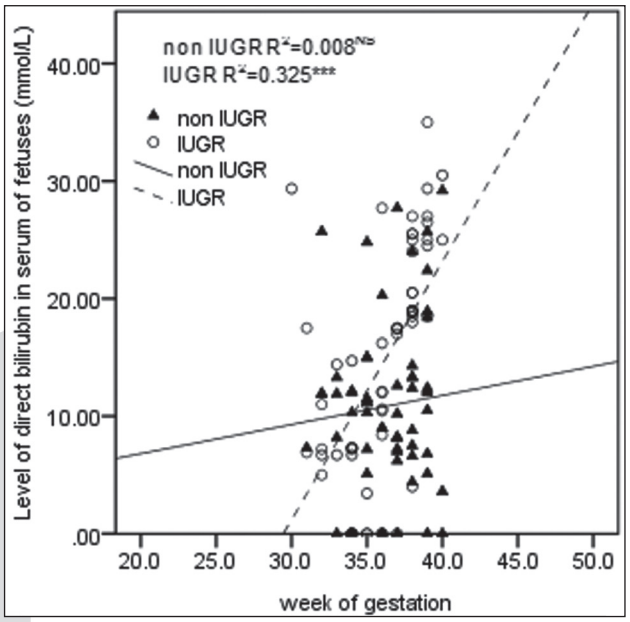

*Figure 3. Ratio of FLL / AST in non IUGR and IUGR groups (*** p< 0.001)*

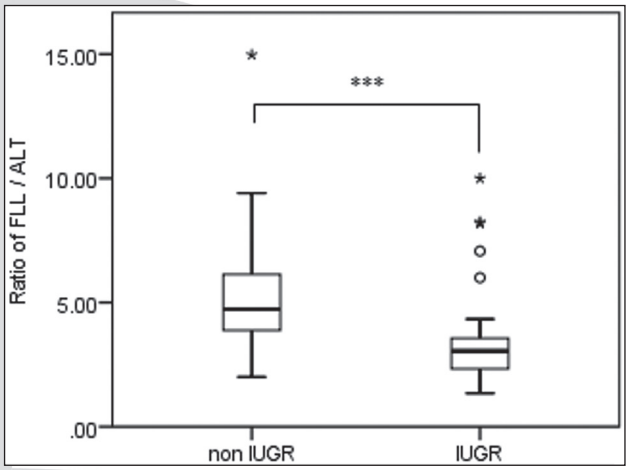

*Figure 4. Ratio of FLL / ALT in non IUGR and IUGR groups (*** p< 0.001)*

Discussion

In this prospective study, we evaluated ultrasound fetoplacental parameter FLL in fetuses with IUGR and non IUGR and we calculated the ratio of FLL and aminotransferases in serum. In our study, fetuses in IUGR group had higher median value of indirect bililirubin in serum 32.4 (26.4 to 39.0) compared to non IUGR group 27.0 (22.6 to 32.6) but the difference did not reach statistical significance, p> .05. In a fetus with IUGR there was negative correlation between gestational age and levels of indirect and direct bilirubin.Fetuses in IUGR group had statistically significant higher

median value of direct bililirubin in serum 16.6 (6.8 to 23.1) compared to non IUGR group 10.4 (6.9 to 13.3) $p< .05$ *(Table 1)*. Because of liver perfusion is reduced to 30%, fetuses with IUGR have elevated AST and ALT aminotransferases as a result of hypoxic liver cell injury.In our study, ratio of FLL / AST and ratio of FLL / ALT were smaller in IUGR compared with non IUGR fetuses, because of lower values of FLL and higher values of aminotransferases in serum of fetuses with IUGR. Murao et al., concluded that the FLL in SGA fetuses was smaller than in appropriate-for-gestational-age (AGA) fetuses and that FLL measurements may be useful in the detection of SGA (12). Deter et al., suggested that the most appropriate growth parameters of 3D organs would be weight, volume, and surface area (13). Kuno et al., concluded that liver volume (LV) may be a useful measurement for diagnosing SGA fetuses in the mid to late third trimester (5). Our findings suggest thatthe diagnostic approach to IUGR should integrate information from maternal history and physical examination with information from laboratory findings and sonographic evaluation of the fetus, placenta and amniotic fluid.

Conclusion

Ratio of FLL / AST and ratio of FLL / ALT werelower in IUGR compared with non IUGR fetuses. In a fetus with IUGR there was negative correlation between gestational age and levels of indirect and direct bilirubin.

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Insulin Resistance and AMH Good Surrogate Diagnostic Markers in the Phenotypes of Polycystic Ovary Syndrome

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Abstract

Introduction: According to the Rotterdam consensus there are four phenotypes of Polycystic Ovary Syndrome (PCOS): phenotype A, B, C, and D. Differences among them have not been investigated in great detail. The aim of this study was to determine the validity of the diagnostic parameters: homeostasis model assessment for insulin resistance (HOMA-IR) andserum anti-Müllerian hormone (AMH) levels in the phenotypes of PCOS.

Materials and Methods: We conducted a retrospectively-prospective case-control study. 90 women in total were divided into four phenotype subsets based on the main characteristics of the PCOS, as following: phenotype A (polycystic ovaries PCOM) + oligoovulation or anovulation (OA) + hyperandrogenemia [HA], phenotype B (OA+HA), phenotype C (HA+PCOM), phenotype D (HA+PCOM). AMH and other hormone levels were measured from serum, HOMA-IR was determined by calculation according to the formula: HOMA-IR = fasting insulin (μlU/ml) x fasting glucose (mmol/L) / 22.5 (ref.<2.16). The main results of this investigation were the serum concentrations of AMH and HOMA-IR in the PCOS phenotypes.

Main results: The mean values for HOMA-IR (3.1 vs.1.8, p <0,04), and AMH (6.8,1 ± 3.4 ng/ml vs. 2.4 ng/ml, p<0.05) were significantly elevated in patients with PCOS in comparison with the patients without the PCOS. Mean values of HOMA-IR were 3.2±1.8 in phenotype A; 2.8±1.4 in phenotype B; 2.5±1.2 in phenotype C; and 3.2±1.6 in phenotype D. Mean value of AMH in serum was 9.50 ± 6.1 ng/ml in phenotype A; 8.02 ± 6.2 ng/ml in phenotype B; 7.9±2.7 phenotype C,and 3.06 ± 2.4 ng /ml in phenotype D.

Conclusions: AMH and HOMA-IR are good side parameters for the PCOS diagnosis, but they are not significant in differentiation among the variety of phenotypes of PCOS.

Key words: Polycystic Ovary Syndrome, HOMA-IR, AMH, phenotypes.

Introduction

Polycystic ovary syndrome (PCOS) is a frequent problem in reproductive endocrinology, with te prevalence of about 15-18%, according to the ESHRE/ASRM diagnostic criterion (1,2).

In the last decades it became very clear that the PCOS is a complex endocrinopathy, even more so than hairiness or infertility (3). The majority of women with the PCOS are resistant to insulin (4,5). Central or visceral obesity is associated with a greater insulin resistance (6,7). Women with PCOS have a greater risk of metabolic syndrome (8), hypertension, abnormal metabolism of glucose, increased risk of developing a cardiovascular disease (9). They have a greater miscarriage prevalence, pregnancy hypertension, preeclampsia, gestational diabetes mellitus (GDM), complicated and premature child-births (10). Based on the Rotterdam consensus 2003, the three diagnostic criterion for PCOS were proposed: oligo-ovulation/anovulation (OA), clinical/or biochemical hyperandrogenemia (HA), and polycystic ovarian morphology (PCOM). The diagnosis is confirmed when there are two out of three criterions present, after exclusion of the possibility of the diseases linked with the overproduction of androgens (like PCOS) (11). PCOM varies during the menstrual cycle and when oral contraception is used, which decreases a confidence in estimating of PCOM (12).

Anti- Müllerian hormone (AMH), also known as Müllerian inhibitory product made by granulose cells of the small anral follicles has an important role in the development of the follicle (13). AMH levels in females is low by the age of eight, increasing rapidly by puberty and maintain their levels by the age of 35, after which they are falling down until the menopause, when the AMH production ceases (14). According to this, AMH is proposed as a marker of PCOS and as a substitute for AFC when diagnosing PCOM (15). The levels of AMH are positively correlated with free testosterone, androstendione and free androgen index (FAI) in women with PCOS and non-PCOS with the PCOM-like (16). The study of Dewailly et al. have shown that it can be used as a surrogate marker for a classic hyperandrognemia (17). The Aim of this study was to determine the diagnostic importance of the AMH and HOMA-IR parameters in diagnosing phenotypes of PCOS.

Materials and Methods

A retrospective-prospective case-control study. This study encompassed the women of reproductive age (18-35), from the territory of Bosnia-Herzegovina, who gave their consent for participation in it and who were examined in the Private Health Unit Dr. Hajder between January 2012 and December 2015. The examined group consisted of women selected according to the Rotterdam diagnostic criterions for PCOS (11). The patients with PCOS were divided by 4 phenotypes [A / B / C / D] (11). The study excluded the patients who received hormonal therapy within the three months prior to its beginning, older than 35, FSH>25 mIU/mL, and 17a-OH-P >1.5 ng/mL.The criterions for the PCOM inclusion were ultra sound findings of minimally 12 follicles with diameter of 2-9 mm in each ovary and/or increase of ovarian volume to the minimal size of 10 cm^3 (17).

The women in the control group were healthy volunteers with the normal ovulatory cycles (28+2 days), with the blood progesterone level of 10 ng/ml in the two consequent cycles, without signs of hyperandrogenemia, and with a healthy ultrasound appearance of the ovaries. The hormone blood tests were done in the early follicularphase, between the 3rd and 7th day of the menstrual cycle, after a spontaneous menstruation.

The women with PCOS who did not have a spontaneous menstrual cycle within 90 days were treated with 2x10 mg of micronized progesterone for 5 days (Utrogestan, Faranlaboratorijes Tories, Athens, Greece) to invoke the bleeding, and the blood samples were collected after that.

Definition

Hirsutism is defined based on the Ferriman-Gallwey (FG) score greater than 8, ovulatory dysfunction was defined if less than 8 menstrual cycles in a year or lutein progesterone of less than 9.54 nmol/L, menstrual dysfunction if the cycles span is longer than 35 days and less than 21 days (18). Metabolic syndrome is defined by the recommendation of International Diabetes Federation (IDF). Biochemical hyperandrogenemia is defined if the total testosterone is > 2.08 nmol/L, free testosterone is greater than 6.94 pmol/L, DHEAS greater than 7.8 umol/L. Total testosterone greater than 5.2 nmol/L and greater than DHEAS 20.8 μmol/L suspected to active androgenic tumor. Elevated serum basal 17-OHP value greater than 9.1 nmmol/L and the increased value of 17 OHP after stimulation with ACTH greater than 30.3 nmmol/L is considered NCAH. AMH of the serum is measured by Gen II enzyme-linked imunosorbent assay (ELISA) ng/ml. HOMA-IR >2.16 were a sign of IR and insulin sensitivity, and are counted by the formulas. FAI was counted by the formula = (total testosterone nmmol/L x 100 T / SHBG nmmol/L), FAI > 3 indicates hyperandrogeny (19). TVCD criteria: more than 12 follicles, the size of 2-9 ml, 10 ml larger volume, increased ovary stroma (formula = π / 6 (DB1xDB2xDB3).

Laboratory assays

Insulin (μlU/ml) was determined by RIA (direct radioimmunoassay) on Wallec automatic counter (Wizard) Turku Finald Company. The INSI-CKIT Irma firm DiaSorin, Italy was used. Insulin sensitivity was calculated by the formula: HOMA-IR = fasting insulin (μlU/ml) x fasting glucose (mmol/L) / 22.5 (ref. < 2,16) (20). Insulin, DHEAS, 17-OHP, SHBG, total testosterone were measured by, determined by RIA (direct radioimmunoasay) on Wallec automatic counter (Wizard) Turku Finald Company. The original IRMA kits for individual hormone companies IMMUNOTHEC a Beckman Coulter Company, France were used. Estradiol, Pg, FSH,

LH, testosterone were determined by the method of the apparatus Fluroimmunoassay Wallace, DELFIA FLUROMETER. The original DELFIA kits for individual firms hormone Turku, Finald were used. Glucose in the hospital conditions was measured by enzyme-colorometrics method (Glucose GOG-PAP) on the unit VP Super System, diagnosis Division, USA. The ultra-sound measurements were taken by using a GE Voluson E8, with a transvaginal sonde of 5 MHz.

Results

This clinical study involved 90 infertile women of reproductive age between 20 and 35, selected by the Rotterdam criterions. Phenotype A was represented by 41 (45.5%), phenotype B by 28 (31.1%), phenotype C by 9 (10.1%), and phenotype D by 12 (13.3%). The mean value of the age for the PCOS group was significantly higher (31.1 vs. 28.2, p<0.01) compared to the non-PCOS group. The PCOS women had significantly higher value of BMI (28.4 vs. 24.1, p<0.001), HOMA-IR (58% vs. 12%, p<0.01), oligo/anovulation (87% vs. 22%, p <0.005), hyperandrogeny (58% vs. 5%, p <0.05), PCOM (72% vs. 18%, p <0.01) compared to the control group. There were no significant differences in starting of menarche between the groups (Table 1).

This study found that the PCOS group had a trifold value of the serum AMH level in comparison to the control, normo-ovulatory group without PCOS.The mean AMH level was (9.13 ± 2.6 ng/ml vs. 3.1±1.6 ng/ml, p<0.002) and was significantly higher in the PCOS group compared to the control group (Table 1). Level of serum AMH in the PCOS group was significantly higher for all PCOS phenotypes (p<0.05) in comparison to the control group.The PCOS phenotypes: A, B, and D had significantly higher values (p<0.05) of AMH compared to the phenotype C. There were no significant difference among the PCOS phenotypes A, B, and D in the levels of AMH (Table 2).

PCOS patients with the BMI ≥ 25 kg/m2 had significantly lower value of AMH (7.6±3.4 ng/mL vs. 10.1±3.2 ng/ml, p<0.03) compared to the PCOS patients with the BMI <25kg/m2. (Table 3).

Insulin resistance (IR) was present in the 58% women with the PCOS. The PCOS group had the fasting insulin values of 12.1±1.6 vs. 7.8±2.6, p<0.03, and HOMA-IR (3.1±3.6 vs. 2.1±3.6, p <0.04), which was considerably higher than for the non-PCOS patients (Table 1).

Mean HOMA-IR values for the PCOS group were significantly higher for all phenotypes of PCOS (p<0.05), compared to the non-PCOS women. PCOS women with the BMI ≥ 25 kg/m2 had significantly higher mean value of HOMA-IR (5.6±3.1 vs. 2.4±2.6, p<0.05), fasting plasma insulin (FPI) (12.2±3.1 vs. 9.8±2.9, p<0.05) when compared to the women with the BMI<25kg/m2. There were no significant differences among the PCOS phenotypes (A vs. B; A vs. C; A vs. D; B vs. C; B vs. D; C vs. D)

Table 1. Baseline clinical and hormonal characteristics of PCOS patients

Variables	PCOS	non-PCOS	p-value
Age (years)	31.1 ±4.6	28.2 ±5.3	0.01
Age of menarche	13.8 ± 2.3	1259 ± 2.4	0.8
BMI (kg/m^2)	28.4 ±4.3^{,a}	24.1±2.1 ^{c}	0.001
Insulin resistance (%)	58%	12%	0.02
Oligo/anovulation (%)	87%	22.%	0.005
Polycystic ovaries (%)	72.%	18%	0.01
Hiperandrogenism (%)	58%	5%	0.05
Central obesity/obesity (%)	57%	18%	0.002
AMH (ng/ml)	9.13±2.6	3.1 ±1.6	0.002
HOMA-IR	3.1±3.6	2.1±3.6	0.04
Insulin (μIU/ ml)	12.1±1.6	7.8±2.6	0.03
Glucose (mmol/l)	4.7±0.4	4.6±0.6	0.09

Note: values are the mean ± SD, or as number (%); PCOS, Polycystic Ovary Syndrome; BMI, body mass index; AMH, anti-Mullerian hormone; HOMA-IR, homeostasis model assessment for insulin resistance index; p-value<0.05, statistical significant for PCOS vs. non- PCOS.

Table 2. Comparison between the different phenotypes of PCOS and the non-PCOS.

Variable	PCOS (total population) (n=90)				Non-PCOS (total population) n=30 (100%)
	Phenotype A (OA+HA+PCOM) n= 41 (45.5%)	Phenotype B (OA+HA) n=28(31.1%)	Phenotype C (HA+PCOM) n=9(10.1%)	Phenotype D (OA+PCOM) n=12(13.3%)	
Age (years)	28.5±5.20	27.3±5.1	28.3±4.9	26.8±5.1	27.6±5.2
BMI (kg/m^2)	26.9±5.7[a]	26.8±6.1[a]	26.2±5.5[a]	26.3±6.2[a]	24.7±6.4
FSH (IU/L)	5.7±1.6[a,c]	5.9±1.6[a]	6.4±1.5[a]	6.1±2.1[a]	7.3±2.4
LH (IU/L)	8.7±4.2[a,b,c,d]	7.1±5.4	6.1±3.9	6.5±4.1	5.8±2.6
Luteal progesteron (nmol/L)	3.6±2.6[a,c]	4.1±3.6[a,e]	12.6±7.1[g]	6.7±4.9[a]	12.6±5.2
Testosterone (nmol/L)	2.8±0.9	2.6±0.8	2.5±1.1	1.5±0.5	1.4±0.3
SHBG (nmol/L)	37.2±18.6[a,d]	37.9±21.3[a,f]	44.6±19.1[a]	54.2±22.6[a]	68.4±34.6
FAI	10.1±6.5[a,b,c,d]	8.6±5.2[a,f]	7.1±4.1[a,g]	3.6±2.9[a]	2.3±0.9
Glucose (mmol/L)	5.2±0.8	5.1±0.6	5.4±0.5	5.2±0.6	5.3±0.7
Insulin (μIU/L)	14.12±3.1[a]	12.42±3.2[a]	10.42±2.9[a]	13.03±3.9[a]	9.92±3.8
HOMA IR	3.2±1.8[a]	2.9±1.4[a]	2.7±1.2[a]	3.2±1.6[a]	2.1±1.2
AMH (ng/mL)	9.13±2.6[a,c]	**7.9±2.7**[a,e]	4.54±1. 6[a,g]	7.6±1. 7[a]	3.1±1.6
Ovarian volume (cm^3)	9.5±2.1[a,b,c]	5.4±1.8[a,e,f]	8.4±2.6[a]	8.2±3.1[a]	5.2±1.5
Ovarian follicles (FNPO)	14.1±3.7[a,b]	6.8±2.4[e,f]	12.1±2.6[a]	12.6±3.1[a]	6.4±1.8

Note: Values are the mean ± SD, BMI, PCOS, Polycystic Ovary Syndrome; FSH, follicle-stimulating hormone; LH, luteinizing hormone; SHBG, sex hormone-binding globulin; BMI, Body mass index; AMH, anti-Müllerian hormone; FNPO, follicle number per ovary; HOMA-IR, homeostasis model assessment for insulin resistance index; .[a] P<0.05 for phenotypes vs. non-PCOS; [b] P<0.05 for phenotypes A vs. phenotipe B; [c] p<0.05 for phenotypes A vs. phenotipe C; [d]P<0.05 for phenotypes A vs. phenotipe D; [e] P<0.05 for phenotypes B vs. phenotype C; [f] P<0.05 for phenotypes B vs. phenotype D; [g] P<0.05 for phenotypes C vs. phenotype D; NS, not significant.

in the levels of HOMA-IR (Table 2). Mean values of FPN were significantly higher for the all PCOS phenotypes (p<0.05) in comparison to the non-PCOS group. The PCOS group did not exhibit significant differences among the phenotypes (A vs. B; A vs. C; A vs. D; B vs. C; B vs. D; C vs. D) in the levels of FPI (Table 2). Mean FAI values vere significantly higher for all PCOS phenotypes, (p<0.05) compared to the control, non-PCOS women. Among the following phenotypes of the PCOS group, there were significant differences (A vs. B; A vs. C; A vs. D; B vs. D; C vs. D), while there were no significant differences between the women with the PCOS phenotypes B vs C. (Table 2). The ovulatory women with the PCOS phenotype C had significantly higher values of luteinizing progesterone compared to those with the PCOS phenotypes A, B, and D, while there were no differences with the non-PCOS group. The non-ovulatory PCOS with phenotypes A, B, and D had considerably lower (p<0.05) levels of luteal progesterone. The anovulatory PCOS phenotypes A, B, and D had a significantly lower level (p<0.05) of luteal progesterone compared to both non-PCOS and PCOS, phenotype C. Polycystic ovarian morphology (72.% vs. 18%, p<0.01) was significantly more present in the PCOS women, compared to the non-PCOS. The PCOS women had a significantly higher mean value of the ovarian volume (9.4±2.1cm3 vs. 5.1±1.6 cm3, p <0.01), FNPO (12.4±3.1 vs. 6.3±1.6, p <0.01), in comparison with the non-PCOS women. PCOS women with the phenotype B had significantly lower (p<0.05) values for the ovarian volume and FNPO in comparison to PCOS phenotypes A, C, and D.

Discussion

The workshop, under the auspices of ESHRE (European Society for Human Reproduction and embryology) and ASRM (American Society for Reproductive Medicine) held in Rotterdam in the year 2003, proposed a new definition for the PCOS. By this consensus, PCOS was defined as a syndrome if the two out of the three criterion were met: OA, HA, and PCOM with the exclusion of the PCOS like (congenital adrenalhyperplasia, tumors of ovary and adrenal glands excreting androgens, Cushing's syndrome, hyperthecosis). The

Table 3. Baseline clinical and hormonal characteristics of PCOS patients according to BMI

Variables	PCOS BMI ≥ 25 kg/m²	PCOS BMI < 25 kg/m²	p-value
Number (%)	57%	43% ±5.3	0.08
BMI (kg/m²)	28.4 ±4.3	24.1±2.1	0.005
Free androgen index	3.52±3.0	6.20±3.9	0.003
DHEAS (μg/dL)	194.8±80.1	240.6±73.9	0.004
Testosteron	0.47±0.4	0.74±0.6	0.001
FAI	8.4±3.4	6.2±2.4	0.003
AMH (ng/ml)	7.6±3.6	10.1±3.2	0.03
HOMA-IR	5.6±3.1	2.4±2.6	0.05
Insulin (μIU/ ml)	12.2±3.1	9.8±2.9	0.05
Glucose (mmol/l)	4.8.±0.3	4.3±0.4	0.09

Note: values are the mean ± SD, or as number (%); PCOS, Polycystic Ovary Syndrome; BMI, body mass index; AMH, anti-Mullerian hormone; HOMA-IR, homeostasis model assessment for insulin resistance index; p-value<0.05, FAI, free androgen index; statistical significant for PCOS vs. non- PCOS.

four PCOS phenotypes were suggested, which is today a matter of consideration. The same consensus did not include IR and AMH into the earlier Rotterdam criterions from the year 2003 (20,21).

The third consensus from the year 2012 the PCOS was re-defined. It is an endocrine disorder in the reproductive age of woman, characterized by a menstrual dysfunction, anovulatory infertility, hyperandrogenemia, and insulin resistance (22).

IR is the main pathophysiological cause of PCOS development. It is caused by the effects of TNF-alpha product of the visceral adipocyte which changes tyrosine phosphorylation into serine phosphorylation, making IRS-2 which in turn decrease production of the glucose transporter GLUT-4. The created IR is followed by a compensatory hyperinsulinemia. The hyperinsulinemia induces hypothalamus, ovaries and suprarenal glands to androgen excretion (23). Insulin resistance is pathologically involved in the reproductive and metabolic abnormalities in women with POCS (6). Increased insulin resistance is a prominent characteristics of PCOS (25). The results of this study have pointed that the insulin resistance (HOMA-IR) is present in the patients with PCOS. All phenotype groups had significantly elevated HOMA-IR, compared to the non-PCOS group. The results of this study corroborate with the earlier findings in the IR studies (24,25,26,28). All previous studies on HOMA-IR showed that the PCOS patients had HOMA-IR, with small differences among the phenotypes. The differences are mainly there due to the differences in race, in geographical areas and in the way of living. Hwang et al. reported the IR presence in the PCOS patients. HOMA-IR, fasting insulinand (postprandial?) insulin after 2h were significantly higher in comparison to the control group. The increase in AMH is not followed by elevation of HOMA-IR and androgens. AMH was significantly greater, while FAI was significantly lower in the patients with the BMI >25 kg/m². There were no differences for the values of HOMA-IR among the PCOS phenotypes (25). Panidis et al. reported that HOMA-IR was significantly higher ($p<0.01$) values in the PCOS patients when compared to the control group. IR was significantly present in the phenotypes A, B,and D, while missing in the phenotype C. Phenotype A is more associated with IR and HA than phenotype B. Phenotypes B and D are associated with the obesity and IR, while phenotype C was not associated with IR (26). Results of this study indicated that AMH was significantly higher in the patients with PCOS, for all four phenotypes, while there was no differences among the phenotypes. All earlier studies indicated that AMH was significantly present in all PCOS phenotypes, with the greatest levels in phenotypes A and B (24, 26, 27, 28, 29, 30). Hwang et al. reported that AMH was significantly increased in the PCOS women, and that the high level of AMH is not a predictor of PCOS phenotypes. The patients with the BMI>25 kg/m² had a negative correlation of AMH with androgens. Increase in AMH is not followed by an increase of androgens and HOMA-IR. The phenotype group A exhibited a significantly greater level of Dewailly et al. reported that HOMA-IR was significantly higherin the PCOS phenotypes

A, B,and D. The cut-off AMH in the phenotype groups A, B andD >28 pmol/L was a diagnostics marker for PCOS , PCOM and PCOM- like. AMH was significantly higher in the phenotype groups A, B and D, compared to the control group, with the greatest level in the phenotype D (27). Wiwekoet al. reported that the mean value of AMH significantly greater (9.5 vs. 3.5, p< 0.001 in the PCOS group, compared to the non-PCOS. The greatest values for AMH were found in phenotypes A and B, while the greatest rate of occurrence is that for the phenotype D (63%). They also reported that the cut-off value of 4.45 ng/mL is a valid one for the diagnosis of PCOS with specificity of 76.1% and sensitivity 74.6 % (28). Nardo et al. Published tha HOMA-IR in the non-overweight patients with PCOS was significantly higher (p< 0.033), and so was AMH (6.1 vs. 1.9, p<0.001), compared to the control, non- PCOS group. (29)

Sahmay et al, in their study on 251 PCOS women found that the AMH level was 9.50 ng/ml for PCOS type A , PCOS type B had 8.02 ng/ml, 3.06 ng/ml for type C, and type D PCOS measured 3.06 ng/ml. AMH, FPNO, Testosterone, LH, but there was no difference in the HOMA-level compared with the control group without PCOM-like (30). Eilertsen et al. Reported for the AMH cut off threshold above od 20 pmol/L as a good parameter for diagnosing PCOS-Rotterdam and PCOS-AES. AMH > 20 pmol/L was present in phenotypes A, C and D, also in women with either one criterion (OA) or PCOM-like. AMH less than 20 pmol/L was in the non- PCOS and phenotype B (OA+HA) (31).

Dewailly et al. reported that the three phenotype groups of PCOS and PCOM patients as well as in the PCOM-like which did not have PCOS cut-off value had the value of AMH >28 pmol/L. In the three groups with PCOS, with PCOM, and control group with the PCOM-like, AMH, HOMA-IR, FPNO lewels were significantly higher compared to the control group (27). The results of this study indicated that the phenotype percentage with PCOS was: phenotype A; 41(45.5)%, phenotype B 28(31.1)%, phenotype C 9(10.1%) and phenotype D 12(13.3%). Panidis et al. reported the similar frequency: phenotype A; 48.3 %, B; 30.7%, C; 9.7% and D; 11.4% (26). Wiweko et al. published the incidence of phenotypes: A; 29.6%, B; 2.8%, C; 4.2%, D; 63.4% in Indonesian women (28).

Conclusion

The results of this study indicate that the mean values of AMH and HOMA-IR are good surrogate markers of PCOS. The greatest levels of AMH were found in the cases with all three diagnostics criterion present (phenotype A). The AMH levels correlate best with the PCOM. Apart from that, an oligo-anovulation increases elevation of AMH. The level of hyperandrogenemia has little influence on the level of AMH. The most common PCOS phenotype in the Bosnian women ist he phenotype A (OA + HA+PCOM) with the presence of 45.5%, phenotype B (OA + HA) with the presence of 31.1%, while the least presence hasthe phenotype C (ovulatory women).

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A Study of Personality Traits, Mental Health and Work Value between Young Adults From the Continental Plateau Regions and the Plain Geographical Areas

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Abstract

Objective: Regression analysis in personality traits, mental health condition and work value between young adults from the continental plateau region and the plain geographical area.

Methods: Three evaluation forms were used for the study: the Sixteen Personality Factor Questionnaire (16PF), a modified version of the Symptom Checklist-90-R (SCL-90-R), and Work Value Inventory (WVI). 4000 young adults from the continental plateau participated in the study. 1000 young adults from the plain region participated in the study and 936 valid questionnaires were collected (93.6%). After ruling out invalided and uncompleted questionnaires, 3930 valid questionnaires were collected (98.25%).

Results: The modified SCL-90-R showed that young adults from the continental plateau region (n=3930) reported higher levels of symptomatology compared to the plain region group (n=936). The 16PF revealed that young adults from the continental plateau had higher mean score in vigilance, but lower mean score in the rest of 15 subsections than people from the Chinese military norm (n=470). As for work value, the mean scores of internal value and reward in the continental group were the same, and the score of external value was the highest among the three dimensions in the continental group. In the plain group, the mean score from high to low in three dimensions were internal value, external value and reward. The regression analysis of 16 PF towards mental health indicated that the factor of dominance, perfectionism, privacy, emotional stability, and social boldness were correlated with SCL-90-R subscales. The factors of abstractedness and reasoning had correlation with the WVI scores were also noted.

Conclusion: As for young adults, their personality, work value and mental health conditions are shaping from each other. Since personality is considered as a stable factor for an adult, it can be considered as a lead factor for individuals choose to work at different places. In other words, personality characteristics have effects on mental health conditions of young adults who work at continental plateau, as well as on their work values.

Key Points

- Young adults who choose to work at continental plateaus in their early stages of adulthood have a higher risk of reporting high scores on most of the SCL-90-R scales.

- Young adults at continental plateaus are more likely to have personality characteristics that were distinctive to people who work at the plain area, which may have an impact on their work values as well.

- The above findings provide some thoughts for young adults who plan to work at continental plateaus as well as for those who are currently working at continental plateaus.

Key words: continental plateau, plain, SCL-90-R, 16PF, WVI, personality traits

Introduction

Abbreviations used in this article

16PF	Sixteen Personality Factor Questionnaire
ANOVA	Analysis of variance
PTSD	Posttraumatic stress disorder
SCL-90-R	Symptom Checklist-90-R
SD	Standard deviation
WVI	Work value inventory

With the development of society and the boost of the economy, mental health has increased its importance to the public. Much of the research has studied the relationship between personality factors, psychiatric symptoms and work value. Very little research, however, has been conducted in high latitude areas with large sampling. In recent years, though, many assigned work opportunities at continental plateaus are physically and mentally challenging for young adults who have been working there given the environmental conditions of low oxygen, a dry climate, intensive ultraviolent rays, and lack of transportation and interaction with the outside. Given these facts, it is meaningful to conduct research evaluating the potential risk of mental illness, such as PTSD. Better consideration is necessary when selecting candidates before they head to plateaus, both to assess occupational value and to provide effective interventions for young adults who have experienced psychiatric difficulties at continental plateaus. The literature review of the mental health condition of young adults from continental plateaus compared with Chinese military norm indicated that the young adults from continental plateaus had overall worse mental health conditions than the Chinese military norm. The Chinese military norm, however, was constituted by Wang in 1999, which was not updated in 15 years. Therefore, comparisons between young adults from continental plateaus and from plain regions were made in this study. This study aims to provide a better understanding of young adults' mental health conditions and personality characteristics, which might help develop future promising intervention plans that improve militaries' psychological diathesis and gradually improve their work effectiveness.

The literature on the psychiatric symptomatology of young adults from plateaus shows that their self-report of SCL-90-R scores were high among all 9 factors. Except for the aspect of hostility, young adults who have just started work at continental plateaus reported significantly higher scores in all aspects of SCL-90-R (Zhang et al., 1998). Compared to young adults from plain areas, young adults from continental plateaus have more severe symptoms in the areas of depression, anxiety, phobic anxiety, obsessive-compulsive and somatization. This is partly due to the climate and environmental conditions of continental plateaus. Wang, et al. (2000) also supported this theory. The literature on personality analyses of staff who worked at continental plateaus reported a variety of differences (Jun & Tian, 2014). In Wu's Evaluation and Analysis of 16PF Personality Factors of Young adults Working *in Coastal and High Altitude Areas,* it was found that young adults who worked at continental plateaus reported higher scores under the section of C, G and Q3, but significantly lower scores under the section of M and Q4 compared with young adults from the Chinese military norm (Wu, et al., 2013). From Mao's research *The Analysis of Personality Traits of Young adults at High Altitude Areas* (2012), the data showed that the section of G and Q3 had significantly higher scores. Under the section of M, the lower score was also noted. However, the results of Q3 were contradictory with Wu's research, and the score was much higher than the Chinese military norm's result. Furthermore, there was no significant difference of the two scores under the section of C (Mao et al., 2012).

Many factors have had an impact, such as demographic variables and mental health concerns, on adults' personality traits (Zheng & Yan, 2005). In Li's research (2008), the relationship between personality traits and work value was studied and the result indicated that introversion and extroversion had an influence on work value. Some studies analyzed the correlation between psychological factors and work value. Zhang's research (2007) suggested that self-esteem and motivation are positively correlated to their work values. Other research concluded that self-belief and ideal index have an impact on work value (Du, 2008). Few studies, however, have targeted the research population of young adults from continental plateau regions.

The hypothesis of the study is listed as follows: there are certain connections between personality traits and the development of mental illness for young adults who work at continental plateaus; personality traits are correlated with with work value.

Methods

Subjects

The research was conducted by cluster sampling, choosing staff from three corporations. Among the three corporations, one was located in Tibet, China (over 3000m altitude). According to the Table 1, the other two corporations were located in plain areas where the altitude is less than 900m. In the Tibet group, after ruling out 70 uncompleted questionnaires, there were 3930 young adults from the age group 17-49, with a mean age of 22.50, SD 3.79, who participated in the study and completed the SCL-90 evaluation. Among the 3930 staff, 400 of them participated in the research of 16PF and 375 valid questionnaires were collected (93.75%).

Table 2 suggested that plain group was consisted of 936 valid questionnaires from the age group 17-41, with a mean age of 22.57, SD 3.86. Those participants filled the form SCL-90, with 337 of them completing the 16-PF questionnaire. None of those young adults had been diagnosed with any significant cardiopathy, pulmonary diseases or cerebral disease. None of them had a history of mental illness, and they were cooperative with the research project.

Measures

The Self-reporting Inventory Item 90-R (SCL-90-R), the Cattell Raymond B. Sixteen Personality Factor questionnaire (16-PF) and Work Value Inventory (WVI) have high clinical reliability and validity. Thus, they were chosen as standard tools in the research.

Symptom checklist-90-revision. The modified Self-reporting Inventory Item 90 (Derogatis, 2000), was translated into Chinese, and was applied as the standard tool in the research project. The literature reviews indicated that 5 factors out of 9 in SCL-90-R showed significant differences between continental plateaus and plain regions. Therefore, the young adults were given modified SCL-90-R and only valued five factors - anxiety, depression, obsessive-compulsive, phobic anxiety and somatization, reflecting the psychological symptoms seen in psychiatric patients. This modified test consisted of 52 items out of 90 and assessed the sub-areas of somatization (12 items), obsessive-compulsive (10

Table 1. Demographic information of continental plateau region (n=3930)

Variations	Category	Number	Percentage (%)
Length of work (year)		3.89±4.78	
Occupational category	Manager	275	7.00
	Supervisor	1514	38.52
	Worker	2141	54.48
Nationality	Han	3553	90.40
	Minority group	377	9.60
Marriage status	Single	3534	89.92
	Married	396	10.08

Table 2. Demographic information of plain region (n=936)

Variations	Category	Number	Percentage (%)
Length of work (year)		4.31±3.66	
Occupational category	Manager	32	3.42
	Supervisor	426	45.51
	Worker	478	51.07
Nationality	Han	912	97.44
	Minority group	24	2.56
Marriage status	Single	800	85.47
	Married	136	14.53

items), depression (13 items), anxiety (10 items), and phobic anxiety (7 items). Respondents score 54 items with a 5-point scale (1=”no problem” to 5= “very serious”) to evaluate the degree of the symptoms they have experienced. For each section, the mean of a score above 2 represents a clinical positive, and the higher the mean is, the worse the symptoms the person experiences.

Sixteen personality factor questionnaire. Cattell’s Sixteen Personality Factors Questionnaire (IPAT, 1986) included 16 factors as follows, warmth (A), reasoning (B), emotional stability (C), dominance (E), liveliness (F), rule-consciousness (G), social boldness (H), sensitivity (I), vigilance (L), abstractedness (M), privacy (N), apprehension (O), openness to change (Q1), self-reliance (Q2), perfectionism (Q3) and tension (Q4). Items for each factor were scored on a bipolar scale, and then were added to form global secondary factors. This study used an adjusted version by Zhu and Dai (1988).

Work values inventory (WVI). WVI was selected from *Supper*, modified by Ning in 1970. This inventory divides work values into three dimensions, external factors (have nothing to do with the work itself), internal values (related to the work itself) and reward (includes material income and mental fulfill). There are 15 factors under the three dimensions, and four questions are included under each factor. This questionnaire reflects work values seen in respondents, who scored 60 items with a 5-point scale (1=”not important” to 5= “very important”). In order to prevent random answers or other factors that may cause questionnaires ineffective, 7 items out of 60 were picked as re-test questions. Thus, each questionnaire has 67 items in total. When accounting for final scores, any questionnaire in which one or more re-test question is different than the previous one was considered invalid.

Procedure

The research was conducted by group samples and by the same team of evaluation researchers. Informed consent guidelines from the young adults and supervisors were obtained during interviews. The ethical committee of the Fourth Military Medical University Medical Center accepted the study plan, and all the data was collected on site.

The study was conducted by convenient cluster sampling. In January of 2015, the study group members went to Tibet and conducted study though questionnaires and instruments. Each research team was leaded by an associated professor and made of 5 graduate-level students. All the research members had received related training, including instruction statements, acknowledgement of content, measurement process and so on. In order to provide a non-pressured environment for interviewers, during the measuring process, the supervisors were requested to leave the measuring room. To ensure interviewers answer the questions without interruption, the interviewers left 0.5 to 1 meter space between each other. A research member explained the purpose of the research and matters that needed attention to the interviewers and highlighted anonymity and confidentiality. The interview process took about 30 minutes. There were young adults around to ensure all the questions raised from interviewers were answered.

Before delivering the questionnaires, researchers explained the meaning and details about the research to the testers. During the practice, standard directions and time arrangements were provided. During the group test process, the questionnaires were retrieved immediately after the test.

Results

All the data was performed and analyzed by Microsoft Excel and SPSS 20.0 for Mac. A t-test was utilized to find out the statistical significance and line-regression to disclose relevant relationships between scores of SCL-90-R and 16PF. The measurement data was shown by standard deviation ($x \pm SD$) and the result was tested by one-way ANOVA and post hoc test.

SCL-90-R results

As indicated in Table 3, scores under all items, somatization, anxiety, obsessive, depression, and phobic anxiety from the continental plateau region were higher than from the plain group. Except the subscale of somatization, the remaining subscales of SCL-90-R from the continental plateau region were lower than the Chinese military norm (n=19266).

Table 3. Comparison of SCL-90-R item scores between young adults working at continental plateau and plain (x ± SD)

	Somatization	Anxiety	Obsessive-compulsive	Depression	Phobic Anxiety
Continental plateau (n=3930)	1.60±.65	1.46±.59	1.67±.64	1.49±.61	1.28±.49
Plain (n=936)	1.39±.43	1.27±.38	1.51±.49	1.31±.41	1.18±.32
Chinese military norm (n=19662)	1.55±.57	1.52±.52	1.77±.60	1.64±.60	1.35±.45
t	9.38	9.03	7.15	8.62	5.88
P	.000	.000	.000	.000	.000

*The statistics in the chart were standard variables and only factors with significant statistical meaning were listed. ***p<0.001, ** p<0.01, * p<0.05*

Table 4. Comparison of 16-PF item scores between young adults working at continental plateau and Chinese military norm (x ± s)

	Continental plateau (n=375)	Chinese military norm (n=470)
Warmth	6.46±1.39	9.63±3.17
Reasoning	5.60±1.57	7.98±2.05
Emotional Stability	6.12±1.95	15.16±3.20
Dominance	6.22±1.58	11.18±3.58
Liveliness	7.00±1.77	10.74±3.75
Rule-consciousness	5.95±1.62	13.25±3.25
Social boldness	6.32±1.72	9.95±3.75
Sensitivity	5.32±1.49	11.11±2.80
Vigilance	3.92±1.63	1.12±2.39
Abstractedness	5.11±1.47	12.62±3.20
Privateness	5.96±1.60	8.71±2.56
Apprehension	4.57±1.59	11.03±3.54
Openness to change	4.99±1.47	11.78±2.92
Self-reliance	4.19±1.56	12.75±3.30
Perfectionism	5.74±1.57	12.70±3.04
Tension	5.58±1.65	10.83±3.69

All 16 factors disclosed above had significant statistical difference between the two groups (p<0.001)

16 PF results

Table 4 showed that, except for the subscale of vigilance in which the mean score from the continental plateau group is significant higher, all other 15 subscales of the continental plateau group's scores are significant lower than the Chinese military norm (p< 0.001).

WVI Result

Table 5 showed that the mean scores of internal value and reward in the continental group were the same, and the score of external value was the highest among the three dimensions in the continental group. In the plain group, the mean scores from high to low in three dimensions were internal value, external value and reward.

There was no statistical difference (p>0.05) between the two groups under all subscales. When referring to the importance of different values for the two groups, however, young adults from the continental groups believed that peer relationship, life style, altruism, accomplishment and supervision were the top 5 and the least important factors were security, intellectual, economical income, creativity and management. However, in the plain group, the top 5 important factors were peer relationship, accomplishment, life style, altruism, and independence. The least 5 important factors were economical income, management, work environment, mobility and security.

Table 5. Comparison of WVI between the continental group and plain group

	Continental group (n=375)	Order	Plain group (n=337)	Order
Internal value	12.53±2.69		12.83±2.05	
Intellectual stimulation	12.19±2.94	12	12.58±2.45	9
Altruism	12.94±2.88	3	13.33±2.40	4
Creativity	12.21±3.19	14	12.31±2.83	10
Independence	12.72±2.82	6	13.06±2.35	5
Aesthetic feeling	12.53±2.92	8	12.92±2.55	6
Accomplishment	12.87±2.89	4	13.49±2.23	2
Management	12.15±3.16	15	12.27±2.88	12
External value	12.73±2.55		12.73±2.12	
Work environment	12.53±2.85	7	12.27±2.77	13
Peer relationship	13.24±2.79	1	13.63±2.31	1
Supervision	12.83±2.88	5	12.79±2.54	7
Mobility	12.34±2.93	10	12.23±2.64	14
Reward	12.53±2.63		12.57±2.02	
Security	12.29±2.89	11	11.99±2.69	15
Reputation	12.48±2.92	9	12.61±2.48	8
Economical income	12.24±2.98	13	12.30±2.51	11
Life style	13.12±2.84	2	13.37±2.37	3
Work values	12.86±2.55		12.68±1.96	

Table 6. Regression analysis of 16PF, SCL-90-R and other factors in continental plateau (n=375)

	Somatization	Anxiety	Obsessive-compulsive	Depression	Phobic anxiety
Emotional stability	-.07	-.11	-.12	-.14*	-.05
Dominance	-.96*	-.55	-.47	-.55	-.64
Social Boldness	-1.34	-.62	-.42	-.62	-.84
Sensitivity	-.04	.02	-.00	.07	.04
Privateness	-.08	-.07	-.10*	-.08	-.08
Perfectionism	-.09	-.13*	-.11	-.14*	-.15*
Introversion and extroversion	3.15	1.65	1.22	1.67	2.03
	-.06	-.12*	-.12*	-.15**	-.07
R^2	.10	.15	.16	.17	.11
F	2.07**	3.60***	3.72***	4.16***	2.35**

Regression analysis

According to the literature review, the second factor, introversion and extroversion, also has an impact on mental health conditions (Huang et al., 2005). The regression analysis therefore took the second factor into consideration. Consequently, introversion and extroversion, along with 16 personality factors, were considered as independent variables in the study. The subscale scores of SCL-90-R are considered as dependable variables in this regression analysis.

The results (Table 6) showed that one of the16PF factors, dominance, had a negative correlation ($p<0.05$) with somatization, which indicated that young adults with higher scores of dominance had lower scores in somatization. Perfectionism was negatively correlated ($p<0.05$) with anxiety, which meant that with a higher score of perfectionism, young adults would report lower scores under the subscale of anxiety. The data indicated that privacy had a negative correlation ($p<0.05$) with obsessive-compulsive. The higher privacy score one reported, the lower score of obsessive-compulsive one would report. As for depression, emotional stability, and perfectionism had a negative correlation ($p<0.05$). People who reported a high risk of experiencing depression had a lower score of emotional stability and perfectionism. For the section of phobic anxi-

ety, people who reported higher scores of perfectionism had lower scores of phobic anxiety. This meant that perfectionism had a negative correlation ($p<0.05$) with phobic anxiety.

16 personality factors and the factors of introversion and extroversion were considered as independent variables and dependent variables were scores of WVI (Table 7). Through general linear multiple regression equation, the result indicated that only the factor of abstractedness had a significant positive correlation ($p<0.05$) on both WVI from the continental group and the plain group. Reasoning was the only factor that had a negative correlation ($p<0.05$) with WVI score from the plain group.

Table 7. Regression analysis of personality factors towards WVI

	Continental group WVI	Plain group WVI
Abstractedness	.12*	.11*
Reasoning		-.13*
R^2	.07	.10
F	1.66*	2.08**

*The above chat was noted by standardized coefficients. * p<0.05*

Discussion

Potential factors that contributed to the significantly higher SCL-90 scores under all sections in the continental plateau group might be partly due to the work environment. (Jun & Tian, 2014). When working at continental plateaus, young adults face more pressure physically and mentally given the fact that plateaus contain reduced oxygen levels and limited supplies. Moreover, the transportation limitations and tedious working atmosphere also added up to a high risk of reporting psychiatric concerns. The significantly higher SCL-90 score in the group of young adults who have worked less than a year in continental plateaus demonstrated that the mental challenges they faced had an impact on them to some degree. The psychiatric symptoms of young adults who work at continental plateaus were higher than for staff from the plain group, which matched most of the research of people who work at the continental plateau region (Jun & Tian, 2014; Mao et al., 2012; Wang et al., 2008). As the research dove deeper to study the relationship between psychiatric symptoms and different positions they work in, in the continental plateau group, it indicated that managers reported more psychiatric symptoms than supervisors, and young adults reported the fewest psychiatric symptoms among the three groups. It is suggested that compared with managers and supervisors, young adult workers have less outside factors, such as marriage, or management-level work pressure to consider. The later interview with some managers who participated in the study reported that they tend to spend more time worrying about their work arrangement. High rate of separation with their partners is another reason that could have an impact on their mental health well-being.

There have been numerous research studies on how the environmental impact shaped people's personalities (Jun & Tian, 2014; Mao et al., 2012). It is meaningful to highlight here, that most of the young adults who participated in this research left for the continental plateau in their late teenager years or early adulthood, which are the periods that the personality is still forming and not yet stabilized. The experience of working in a continental plateau environment resulted in differences in their personalities, given the fact that there is a significant disparity in data from the continental plateau and the Chinese military norm in many aspects. Of course, the difference could also be attributed to their peer relationships, family influence, or work pressure and so on (Yang et al., 2005; Thailer et al., 1985; Brown et al., 1999). Other than higher vigilance in the continental plateau group, all other 15 subscales' scores are significant lower than the Chinese military norm ($p< 0.001$). Nonetheless, the Chinese military norm data had been collected over a period of more than 20 years and might lack consideration of the characteristics of young adults nowadays.

Young adults from the continental plateau group paid more attention to their works' external value, as the environment at continental plateau regions requires them to seek support from each other and adapt to the environment there. For young adults from the plain region, environmental factors have less of an impact on their work. Thus, they pay more attention to the work itself and put internal value as their top consideration. As for serviceman, the work itself requires people to devote themselves to their career, while the work reward is not their primary concern. That is

most likely the reason to explain why both groups put reward as their least important consideration.

The regression analysis suggested that a person with high emotional stability, dominance, and privacy and low social boldness and sensitivity would better adapt to the service at continental plateau regions. In contrast, some research showed that the secondary factor, introversion and extroversion, had an impact on mental health condition (Huang et al., 2005). Data from the study did not show correlations between the two factors. This may be caused by the fact that the young adults interviewed in this study come from a continental plateau region. The regression analysis also indicated that the personality trait of abstractedness has positive correlations with work value in both the continental plateau and plain area groups. Additionally, reasoning is another personality factor that is able to have an impact on work values in the plain area. Because this personality trait is stable in individuals, one could apply it to selecting staff and service location arrangements for young adults.

However, this study should be understood with caution due to a few limits. First, this study was conducted by population sampling so the external validity may slightly decrease. As Tibet is a vast territory, the armed forces there are residentially contrasting and far away from each other. The research team experienced traveling for hours but only reached a few young adults. Moreover, the sampling was mainly taken in January, therefore the climate and snow blocked the highway and a few encampments were hard to reach through ground transportation. Therefore, though we collected 4000 samples, it could not include all young adults who have been working in Tibet.

Second, SCL-90-R has a limitation in that the evaluated mental health status could only represent a certain length (roughly a week) of time (Shan, 1998). Cross sectional research cannot represent the overall mental health conditions of Tibetan young adults.

Lastly, people who undertake different types of missions have differing occupational values, and the study did not divide the young adults into different groups based on their occupation, but added the score from all samples together.

As a result, it is meaningful to conduct further research on the care young adults' mental health condition and occupational value especially as they work in some extreme environments. Personality is the deciding factor for one's mental health condition and for work value; and acknowledging one's personality characteristics would help to maintain one's well being mentally and prevent a potential mental health crisis. Through the research project, young adults who participate have a better understanding regarding mental health care. For future research, the project at least gives some suggestions concerning young adults who work and live at continental plateaus.

In a conclusion, the present study suggests that young adults who have worked at continental plateaus reported significantly higher psychiatric symptoms than young adults who work at plain areas and differ in personality profiles from the Chinese military norm. The regression analysis suggests personality traits have correlations with both psychiatric symptoms and work values. The study also provides reference for young adults who choose to work at continental plateaus when we refer to their mental health concerns and work value.

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Abstract

In this paper the instructions for preparing camera ready paper for the Journal are given. The recommended, but not limited text processor is Microsoft Word. Insert an abstract of 50-100 words, giving a brief account of the most relevant aspects of the paper. It is recommended to use up to 5 key words.

Key words: Camera ready paper, Journal.

Introduction

In order to effect high quality of Papers, the authors are requested to follow instructions given in this sample paper. Regular length of the papers is 5 to 12 pages. Articles must be proofread by an expert native speaker of English language. Can't be accepted articles with grammatical and spelling errors.

Instructions for the authors

Times New Roman 12 points font should be used for normal text. Manuscript have to be prepared in a two column separated by 5 mm. The margins for A4 (210×297 mm2) paper are given in Table 1.

Table 1. Page layout description

Paper size	A4
Top margin	20 mm
Bottom margin	20 mm
Left margin	20 mm
Right margin	18 mm
Column Spacing	5 mm

Regular paper may be divided in a number of sections. Section titles (including references and acknowledgement) should be typed using 12 pt fonts with **bold** option. For numbering use Times New Roman number. Sections can be split in subsection, which should be typed 12 pt *Italic* option. Figures should be one column wide. If it is impossible to place figure in one column, two column wide figures is allowed. Each figure must have a caption under the figure. Figures must be a resolution of 300 DPI, saved in TIFF format, width 10 cm min. For the figure captions 12 pt *Italic* font should be used. (1)

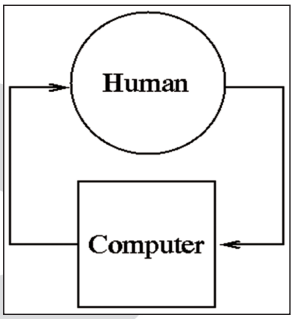

Figure 1. Text here

Conclusion

Be brief and give most important conclusion from your paper. Do not use equations and figures here.

Acknowledgements (If any)

These and the Reference headings are in bold but have no numbers.

References

1. *Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999; 341: 1284–1291.*
2. *Stewart SM, Lam TH, Beston CL, et al. A Prospective Analysis of Stress and Academic Performance in the first two years of Medical School. Med Educ 1999; 33(4): 243- 50.*

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