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CLINICAL SIGNIFICANCE AND UTILITY OF THE HOMA-IR AS PREDICTIVE MARKER FOR PREECLAMPSIA IN THE FIRST TRIMESTER SCREENING

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ABSTRACT. The preeclampsia (PE) is defined as a complication of the hypertension during the pregnancy, having multifactorial characteristics. The PE has a much higher prevalence among the women with diabetes mellitus. Both diabetes and preeclampsia are regarded as major pregnancy both for the mother and the foetus. The pathologic mechanism involving the PE at the women with diabetes mellitus is not fully comprehended. The evaluation of insulin-resistance by the homeostatic model (HOMA-IR) is used to define the insulin-resistance as a predictor for the cardiovascular diseases. The study was performed on pregnant women hospitalised at the Department of Obstetrics-Gynaecology of the Arad County University Clinical Emergency Hospital during 2014-2015. We included in the study pregnant women with pregnancy of 11 to 14 weeks, with or without risk factors for the PE, for whom PAPP-A and insulinemia (for calculating the HOMA-IR) have been dosed, in order to correlate the results with the further development of the PE during the pregnancy.
Keywords: Preeclampsia, Diabetes, PAPP-A, HOMA-IR, Pregnancy 11-14 weeks

INTRODUCTION

The exact origin of preeclampsia stays unknown. The performed studies proved its multifactorial origin. Thus, despite the large number of studies in the area, no available therapeutic approaches have been identified in order to prevent the preeclampsia.

The preeclampsia is one of the most serious and frequent complications occurred during the pregnancy, being also known as main cause for maternal and foetal mortality and morbidity. (Ver Luanni Bilano et al., 2014.; W.E.Ackerman et al., 2014).

The preeclampsia aetiology is not known until now. Several theories have been stated which are not fully accepted and applied into the clinical practice. Recent studies claim that a significant contribution to the preeclampsia aetiology is the imbalance between the angiogenic factors – the vascular endothelial growth factor (VEGF) and the placenta growth factor (PlGF), and the anti-angiogenic ones – the soluble tyrosine-kinase 1 fms-like (sFlt1) and the soluble Endoglin (sEng). (John J. V. mcMurray et al., 2011; Reena Negi et al., 2014; Elnaz Mosaferi et al., 2013; Zohreh Shoar et al.,2013; GuoyingWang et al., 2014; Roger K. Schindhelm et al., 2012).

It has been proven that the major risk factors for preeclampsia are the chronic high blood pressure, the obesity, the hyperinsulinemia and the severe anaemia (Gabriel Choukroun et al.,2011).

Previous studies have reported that women with antecedents of gestational diabetes have a higher risk, of 66% up to 85% higher, for cardiac disease, infarction, and/or for cerebral stroke (Gabriel Choukroun et al., 2011; Yiping Dang and collab., 2013;Magnus Domello et collab., 2013; John J. V.

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McMurray et al., 2011; Nalinne Poolsup et al.,. 2011; Emmanuel Villar et al., 2011).

A state of insulin resistance has been proved in the patients with PE, consequently the women with insulin resistance present a higher risk to develop the PE during the pregnancy. (Akshay S. Desai et al., 2011; Hicham Skali et al., 2013; Pallavi S Hardikar et al., 2012).

All researches performed during the last decades did not bring remarkable or significant improvement to the clinicians' strategy of detecting the preeclampsia before its triggering. Thus, it results the imperious need for predictive markers which are quick in response and easy to use. Early detection means identifying some pathologic changes in the clinical symptomatology of the disease. The large number of publications in the area underlines the increase interest in identifying such biomarkers. Currently, there are attempts to identify some metabolic markers by the combined analyse of the liquid chromatography and the mass spectrometry (Louise C. Kenny and collab.,2010; Anderson U.D. and collab.,2012).

The preeclampsia represents a disorder occurred during the pregnancy after 20 weeks of pregnancy, characterised by hypertension, proteinuria and oedema or occurred postpartum up to 6 weeks since the delivery. The preeclampsia affects both mother and foetus. At worldwide level, the preeclampsia and other pregnancy hypertensive disorders are the main cause for maternal and infantile mortality. These disorders are responsible for annual 76,000 maternal deaths and for 500,000 foetal ones (Preeclampsia foundation, About preeclampsia, July, 2010).

The preeclampsia is one of the most severe and frequent complications occurred during the pregnancy. The preeclampsia aetiology is not known until now. Several theories have been stated, yet not fully accepted and applied in the clinical practice.

The pregnancy hypertension disorders (the preeclampsia) complicate up to 10% of the pregnancies worldwide, being one of the highest causes for maternal and perinatal morbidity and mortality (The American College of Obstetrics and Gynaecology)

The specialised literature describes two forms of preeclampsia that is the mild hypertension (140-159 mm Hg of the systolic blood pressure or for the diastolic one, 90-109 mm Hg, taken twice at, at least, 4 hours distance). The severe hypertension comprises values which are higher than or equal to 160 mmHg for the systolic blood pressure or higher or equal to 110 mmHg for the diastolic blood pressure. (The College of Obstetrics and Gynaecology, 2013)

The incidence of preeclampsia increased a lot in the United States of America since 1990, maybe due to the increase of the predisposing factors, such as the chronic hypertension, the diabetes, and the obesity.

The rates of preeclampsia incidence in the United States of America, Canada and Western Europe range between 5-8%.

In the emerging countries, the severe forms of preeclampsia and eclampsia are more frequent, varying from a minimum of 4% of the total of the births up to 18% in some parts of Africa.

Yearly, ten million women develop preeclampsia at worldwide level. All over the world, about 76,000 pregnant women die every year because of the preeclampsia and of the related hypertensive disorder. It is thought that the number of children dying of these diseases may be of 500,000 deaths per year.

A woman from the emerging countries is seven times more susceptible to develop preeclampsia compared to a woman from a developed country. About 10-25% of these cases lead to mother's death. (Preeclampsia foundation, 2013)

MATERIAL AND METHOD

The study has been performed on pregnant women coming to the Department of Obstetrics of the Arad County University Clinical Emergency Hospital during 2014-2015. We have included in the study pregnant women with pregnancy between 11 to 14 weeks, with or without risk factors for PE. All patients have been submitted to the anamnestic exam based on a pattern resulted from the meta-analyse. Until now, the study comprises 130 pregnant women in the first trimester of pregnancy for which the study questionnaire has been filled in (anamnesis, clinical exam, echography, Doppler echography at the level of the uterine arteries, as well as biochemical investigations), all these data being correlated with data from the delivery. The biological samples have taken from the pregnant women with gestational age of 11-14 weeks, fasting. Complex researches are to be performed to highlight a possible pattern of clinical expression, correlating these data with the values of PAPP-A, and of the HOMA-IR index.

Until now, 83 samples have been analysed by dosing the PAPP-A and the insulinemia (in order to calculate the insulin resistance), which was calculated with the homeostatic model of insulin resistance evaluation (HOMA-IR).

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RESULTS AND DEBATES

Out of the 83 patients for whom the samples have been analysed 7.22% (n=6) had abortion, 10.8% (n=9) were diagnosed with various forms of PIH (pregnancy induced hypertension) who also gave birth, while 81.98 % (n=68) did not develop hypertension while only 51.49% (n=35) of them delivered their children, for the rest the pregnancy is still in progress.

Fig.1 Pregnancies evolution until now

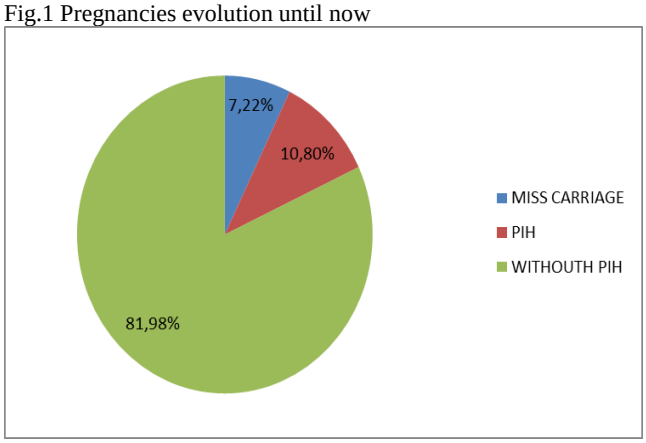
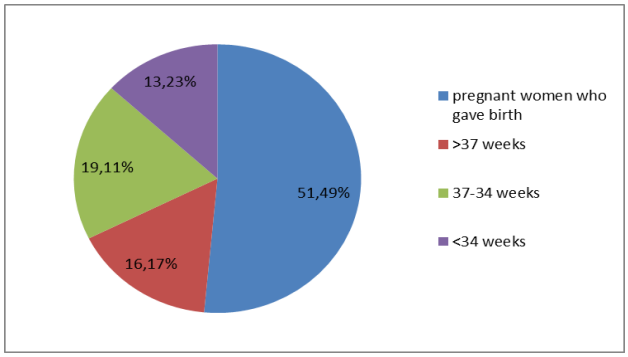


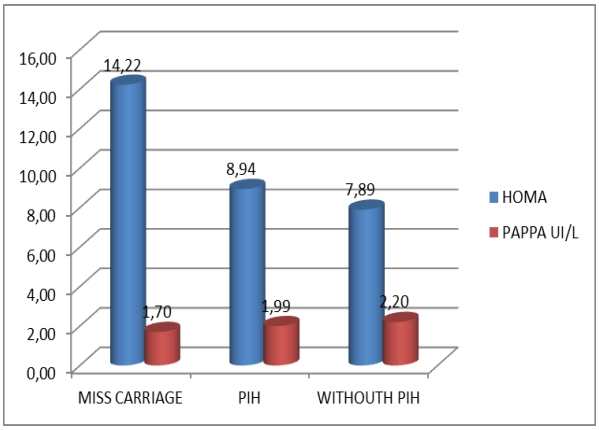
Fig.2 Pregnant women's distribution by current gestational age



Our data showed that the pregnant women who aborted had the lowest PAPP-A values, followed by those developing hypertension, while the pregnant women who had abortions had had the highest HOMA-IR values, followed also by the pregnant women who developed various forms of PIH (preeclampsia). Previous studies also claim the association between a low value of PAPP-A in the pregnancy with the further development of the preeclampsia.(Kalousová et al., 2014.)

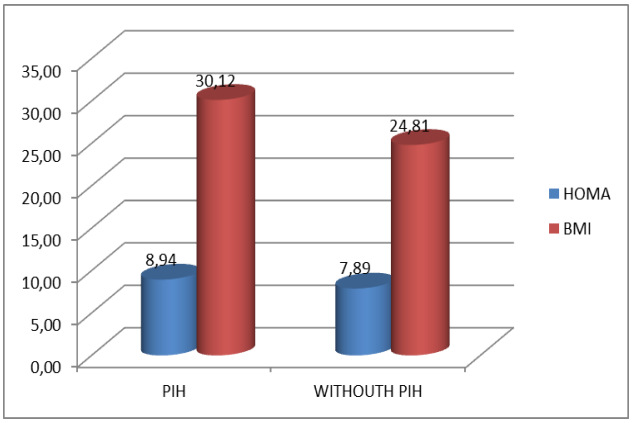
We have observed that the highest values of PAPP-A could be found at pregnant women who did not developed high blood pressure, and also present the lowest vales for HOMA-IR. Consequently, these data show that the increased insulin resistance in association with low values of PAPP-A during the first trimester of pregnancy increase the risk of developing various forms of PIH. The studies on this subject claim that the insulin resistance is involved in the preeclampsia pathogenesis (Wolf M et al., 2002, Farideh Rezaei Abhari et al., 2014)

Fig. 3 Correlations between PAPP-A and HOMA-IR depending on the pathology associated to the pregnancy



The increased insulin resistance, as well as the BMI (body mass index) present values higher among the patients with PIH, compared to the pregnant women who did not develop PIH.

Fig. 4 Correlations between the BMI and the HOMA-IR depending on the pregnancy associated pathology



Among the patients with PIH, the highest frequency is at the primiparous pregnant women

Fig. 5 The primiparous incidence among the pregnant women with PIH

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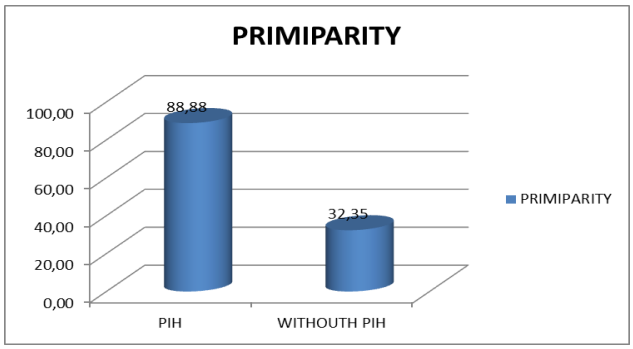

CONCLUSIONS

PAPP- A screening is included in the first quarter , and the values thereof may indicate low risk : intrauterine growth restriction (IUGR) ; Premature birth; Fetal death > 24 weeks ; a spontaneous abortion and preeclampsia . An association of it with increased insulin resistance may lead to increased susceptibility to include a pregnant woman in a - a group at high risk of developing pre-eclampsia and the early diagnosis and appropriate management ONU .

The resulted data show that both an increases insulin resistance and a low value of PAPP-A during the first semester of pregnancy are correlated with the further development of preeclampsia during the pregnancy, however the predictability is as much higher as more factors are taken into consideration such as the BMI and the parity.

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