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Cardiovascular Biomarkers and their changes in hypertensive disorders of pregnancy

D. Gencheva¹, F. Nikolov¹, E. Uchikova², R. Mihaylov^{3,4}, B. Pencheva³, K. Hristova⁵, G. Yamakova², M. Vasileva²

1. Medical University – Plovdiv, First department of Internal diseases, section of Cardiology, Plovdiv, Bulgaria

2. Medical University – Plovdiv, Department of Obstetrics and Gynaecology, Plovdiv, Bulgaria

3. Independent Medical diagnostic laboratory “RAMUS”, Sofia, Bulgaria

4. Medical College “Jordanka Filaretova”, Sofia, Bulgaria

5. Department of Cardiology, MHAT for women’s Health “Nadezhda”, Sofia, Bulgaria, Sofia, Bulgaria.

PURPOSE / OBJECTIVES

Background: Hypertensive disorders of pregnancy are one of the leading causes for fetal and maternal mortality worldwide. Aside from the immediate risk they pose for the pregnant woman, there is significant evidence that women after such a pregnancy have a long-term risk for the development of cardiovascular diseases.

Objectives: To determine the levels of certain biomarkers - Galectin-3, high-sensitivity CRP (hs-CRP), Interleukin-6 (IL-6), indicating cardiovascular involvement in patients with gestational hypertension, preeclampsia and compare them to healthy pregnant women.

MATERIALS & METHODS

A prospective single-centre clinical epidemiological study was carried out at the Clinic of Cardiology and the Clinic of Obstetrics and Gynecology at the University Hospital “Sveti Georgi” Plovdiv, Bulgaria and data was analyzed for 123 pregnant women – 36 with an established diagnosis of gestational hypertension, 37 with preeclampsia and 50 healthy controls. Women with preexisting arterial hypertension, diabetes mellitus, previous cardiovascular pathology and significant systemic disease were excluded from the study. ELISA method was used to determine the levels of Galectin-3, high-sensitivity CRP, Interleukin-6 and Placental growth factor in each of the groups.

RESULTS

The mean levels of placental growth factor were significantly lower in the women with gestational hypertension and preeclampsia compared to the controls (215,89 pg/ml for controls vs. 81,34 pg/ml for preeclampsia and 88.60pg/ml for gestational hypertension), indicating abnormal placentation. Mean levels of Galectin-3 and Interleukin-6 were significantly lower in the control group compared to both of the pathological groups ($p < 0,05$). The gestational hypertension and the preeclampsia group were not statistically different from each other for those two biomarkers.

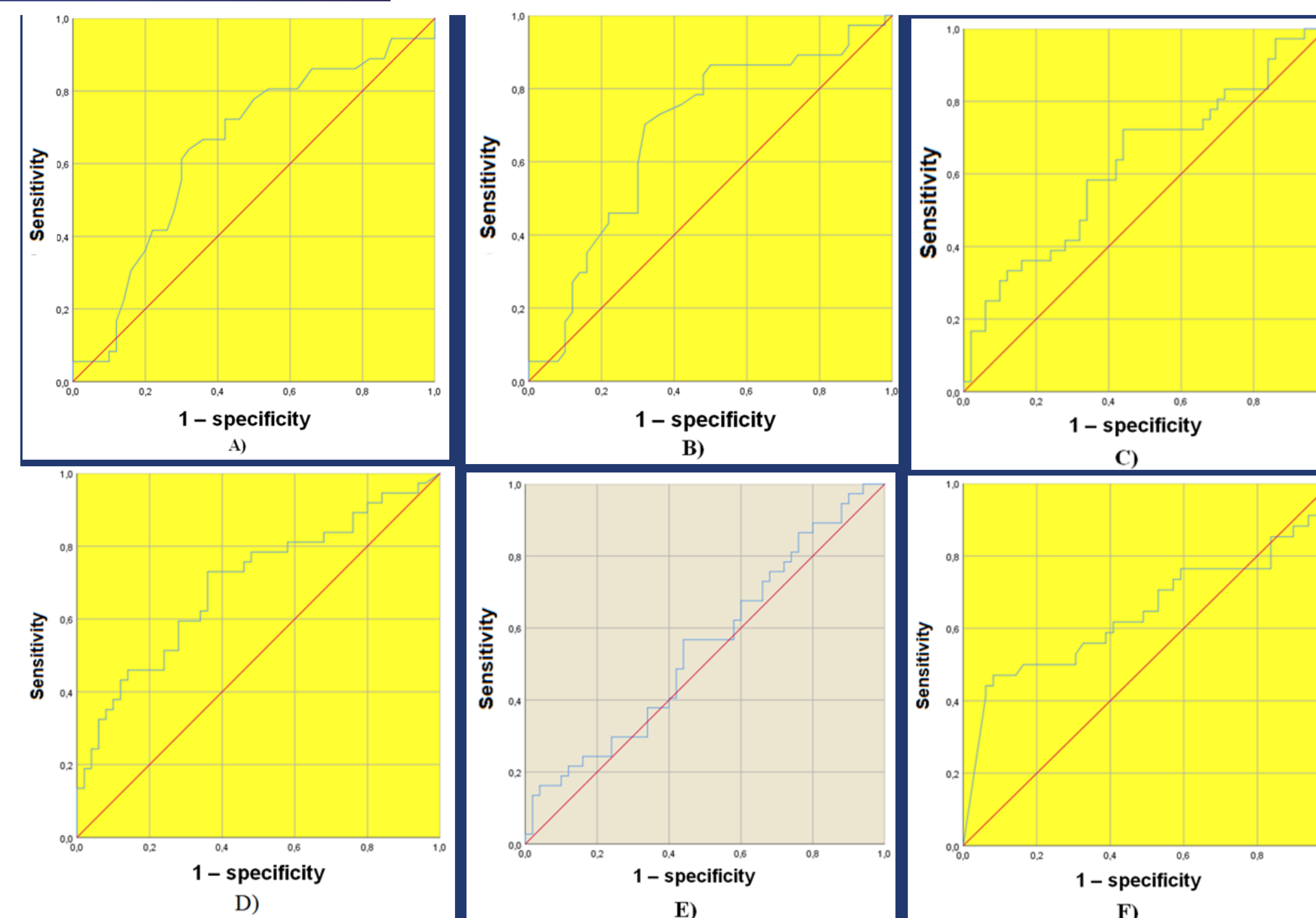


Figure 1: ROC curves of
A) Galectin-3 (AUC 0,646, $p=0,022$),
B) hs-CRP (AUC 0,628, $p=0,043$),
C) IL-6 (AUC 0,648, $p=0,020$) for determining the cut-off values for differentiating between gestational hypertension and the controls
and ROC curves of
D) Galectin-3 (AUC 0,681, $p=0,004$),
E) hs-CRP (AUC 0,548, $p=0,445$) and
F) IL-6 (AUC 0,696, $p=0,002$) for determining the cut-off values for differentiating between preeclampsia and the controls

Table 1: Cut-off values of the studied biomarkers for differentiation between the patients with gestational hypertension and the controls, AUC and values of the validation criteria for screening tests

Biomarker	Cut-off value	AUC	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	% of correct answers
Galectin-3 (ng/ml)	$\geq 7,15$	0,646	67	64	57	73	65
hs-CRP (ng/ml)	≥ 5446	0,628	72	56	54	74	63
IL-6 (pg/ml)	≥ 4	0,648	56	72	59	69	65

Table 2: Cut-off values of the studied biomarkers for differentiation between the patients with preeclampsia and the controls, AUC and values of the validation criteria for screening tests

Biomarker	Cut-off value	AUC	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	% of correct answers
Galectin-3 (ng/ml)	$\geq 7,25$	0,681	70	68	62	76	69
IL-6 (pg/ml)	$\geq 2,82$	0,696	73	64	60	76	68

RESULTS

Mean Galectin-3 level was 6,53 ng/ml in the control group, 7.31 ng/ml in the gestational hypertension group and 7,59 ng/ml in the preeclampsia group. Interleukin-6 levels were 2,77 pg/ml, 5,08 pg/ml and 8,06 pg/ml respectively. High-sensitivity CRP mean levels were significantly higher ($p < 0,05$) only when comparing the gestational hypertension group (6441,12 ng/ml) with the controls (5095,61 ng/ml), but there was no significant difference between the preeclampsia group (5581,02 ng/ml) and the controls and neither between the gestational hypertension and the preeclampsia in our study.

In order to determine the optimal cut-off values of the examined cardiovascular biomarkers for the differentiation between either of the two pathologies and the healthy women, ROC curve analysis was performed. Statistically significant cut-off values could be established for all three of the biomarkers for differentiating the gestational hypertension group from the controls and for Galectin-3 and Interleukin-6 for differentiating between the preeclampsia group and the controls. AUC for the cut-offs (Figure 1) and values of the validation criteria for screening tests are given in tables 1 and 2. Galectin-3, a marker associated with left ventricular hypertrophy, inflammation and fibrosis, had the best accuracy for differentiating the presence of both gestational hypertension and preeclampsia from normotensive pregnancy.

SUMMARY/CONCLUSION

Hypertensive disorders of pregnancy are associated with significant changes in certain biomarkers, indicative of cardiovascular changes. Those findings may explain the elevated risk of arterial hypertension, cerebrovascular disease, ischemic heart disease, diabetes mellitus, venous thromboembolism and other cardiovascular pathologies in women both during and late after a hypertensive pregnancy as already established by multiple large-scale studies. More research is needed on the topic to access the potential of those biomarkers for risk stratification of women with hypertensive disorders of pregnancy in order to improve the multidisciplinary follow-up and care for women.