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CLINICAL VIGNETTE

# ADAM 12 as a prognostic factor of pregnancy induced hypertension — preliminary study

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## INTRODUCTION

The definition of hypertension in pregnancy is based on blood pressure (BP) values obtained in office blood pressure measurements. Hypertension should be diagnosed if systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg is obtained in two independent measurements. Hypertension in pregnancy can be classified as mild (140–159/90–109 mm Hg) or severe (≥ 160/110 mm Hg) [1]. Hypertension in pregnancy affects approximately 6-10% of pregnant women in Europe [2]. PIH is defined per ACOG guidelines after 20 weeks of pregnancy when previous blood pressure was normal [3]. That is why efforts taken to predict PIH before onset of symptoms are of high value to avoid starting treatment as soon as possible and to avoid serious complications like preeclampsia or eclampsia. Treatment of PIH depends on severity and includes anti-hypertensive drugs. Normotension is a term to secure

maternal and fetal well-being. Aim of the preliminary study was to assess if evaluation of meltrin alpha (ADAM 12) between $14^{th}$ to $18^{th}$ week could help to predict development of PIH later in pregnancy.

## METHODS

The study included 105 pregnant women between 14 and 18 weeks of gestation. Following parameters were evaluated: medical history, age, chronic diseases and pregnancy management. The level of ADAM 12 was obtained. Two blood samples are collected from each pregnant woman (approximately 3–5 mL).

## STATISTICAL ANALYSIS

Shapiro-Wilk test was used to verify normality of distribution of continuous variables. Characteristics of continuous variables were presented as arithmetic means and SD, or medians and lower and upper quartiles. Statistical characteristics of qualitative variables were presented in the form of numerical and percentage distributions. Depending on the distribution for intergroup comparisons, continuous variables were analyzed using Student t-test for unpaired variables or the Mann-Whitney U-test. All calculations were performed using Statistica 13.1 software and Excel 2007 with statistical significance set at $p < 0.05$. The study was approved by the Polish Mother’s Memorial Hospital Ethics Committee no. 43/2014. Conflict of interest: none declared.

## RESULTS AND DISCUSSION

Study included 105 women. Mean women' age was. PIH was diagnosed in 3 women (3%). Mean ADAM 12 concentration between 14 to 18 weeks of gestation was 3.85 ± 0.99 vs 4.23 ± 1.30 ng/mL (study vs control) respectively. The difference was not statistically significant ($p = 0.74$) (Fig. 1).

ADAM12 is a proteolytic member of the ADAM proteins that, by splicing, has two forms: a membrane-bound form (ADAM12-L), which has all the domains listed in Fig. 1, including the transmembrane and cytoplasmic domains; and a secreted form (ADAM12-S), which is lacking the transmembrane and cytoplasmic domains [4].

Meltrin alpha is a transmembrane protein that is expressed in various tissues and cell types, including muscle, adipose tissue and the central nervous system. It has been implicated in a wide range of physiological and pathological processes, including embryonic development, tissue repair and inflammation- the processes directly involved in PIH pathogenesis.

To elucidate the role of ADAM 12 in normal inflammation, several in vivo models have been studied. The ADAM 12-deficient tissues showed a significant increase in several inflammatory markers in both RNA and protein levels after analysis. In addition, all ADAM 12-deficient mice models exhibited severe inflammatory symptoms accompanied by neutrophilia in the affected tissues. So, ADAM 12 exhibited a protective role in inflammatory pathogenesis [5].
ADAM 12 was also found to be involved in the trophoblastic cell invasion from the first trimester. It altered the cell-extracellular matrix interactions leading to the reduction of cell adhesion capability and promotion of cell invasion by measuring the first trimester trophoblastic cells. Expression of ADAM 12 was high in cultures of invasive extravillous cytotrophoblast [6]. The processes, both trophoblast invasion and inflammation, are strictly connected with PIH pathogenesis and following preeclampsia development, that is why, studies regarding its value during pregnancy are of high value.  Up to now its role in predicting development of PIH has not been studied. In our preliminary study PIH was diagnosed in 3% of participants respectively. The ADAM 12 concentration was lower in the study group, but with no statistical significance.

As a marker ADAM-12 was studied before to predict preeclampsia and fetal growth restriction. Its lower concentration during the first trimester was seen in women with concomitant preeclampsia. What is more, ADAM-12 concentration showed to be altered in case of pulmonary embolism (possible complications of preeclampsia) [7, 8]. ADAM-12 concentration in case of preeclampsia was also influenced by fetal gender (higher concentration when fetus is male), so future, more profound studies should include fetal gender as a influencing factor [9].

Unfortunately, in our study we did not find a statistically significant difference of ADAM 12 concentration between study group and controls, but that was only a preliminary study, the study group included only 105 cases. ADAM 12 evaluation may have a potential role in

clinical predicting of PIH, but still future studies, with more participants are needed to determine its true clinical value, even if available literature might suggest its potential utility. Considering literature ADAM-12 as a single marker may not reach the aim of predicting preeclampsia, but its value with other markers could probably be used in the future [7].

Article information and declarations

## Ethics statement

The study was approved by the Polish Mother's Memorial Hospital Ethics Committee no. 43/2014.

## Author contributions

Katarzyna Zych-Krekora — literature search, writing the first draft; Oskar Sylwestrzak — literature search, writing the first draft, statistics; Milena Skibinska — collecting data; Maciej Ziebakowski — collecting data; Michal Krekora — study managemnt, collecting data, final version


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## Conflict of interest

The authors declare no conflict of interest.

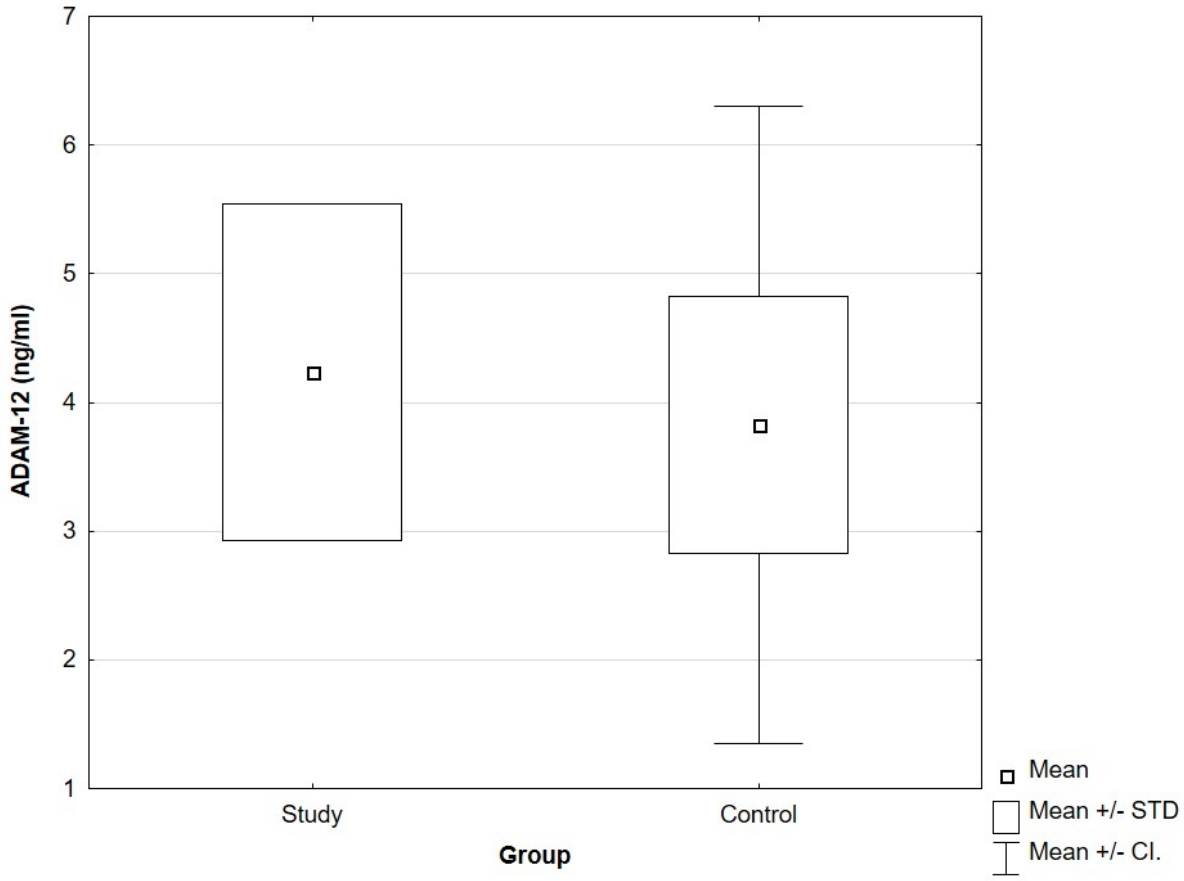


Figure 1. ADAM-12 concentration in the study and control group

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