# fPAPP-A as a biomarker of abnormalities during pregnancy

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## INTRODUCTION

Abnormally low levels of pregnancy-associated plasma protein A (PAPP-A) in serum during pregnancy are associated with a pregnancy complications, such as Down's syndrome and miscarriage. PAPP-A is found in serum in two different forms, as a complex with the proform of major basic protein (proMBP) and as a free active form (fPAPP-A).

It has been suggested that in the first trimester of pregnancy PAPP-A is found in the circulation mostly in free form, but currently used commercial assays measure total PAPP-A, that comprises both fPAPP-A and complexed form. fPAPP-A could possibly be better biomarker of pregnancy abnormalities in the first trimester of pregnancy.

## AIMS OF THE STUDY

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|---|---|
| To determine | The levels of fPAPP-A in serum in the first trimester of normal pregnancy |
| To examine | Whether fPAPP-A is associated with miscarriage |
| To compare | fPAPP-A and total PAPP-A as biomarkers in pregnancy |

## MATERIALS AND METHODS

A serum sample panel (n=197) including women with normal pregnancy (n=160) and women who miscarried (n=37) was analysed with a unique immunoassay, which measures only the free form of PAPP-A (Fig 1). This immunoassay has been developed at the Biotechnology Unit of the University of Turku. The serum samples were collected for a prospective early pregnancy (PEP) cohort in Denmark in 2016 and 2017, during weeks 4-15 of pregnancy.

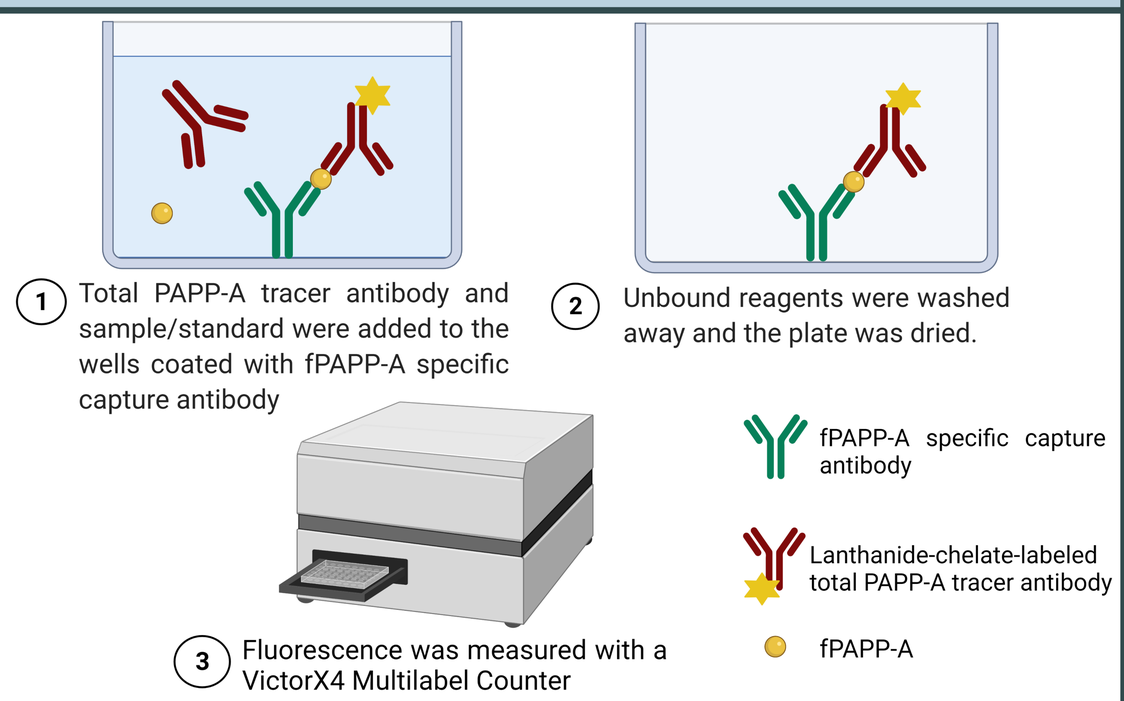


Fig 1. Protocol of the used immunoassay.

## RESULTS AND CONCLUSIONS

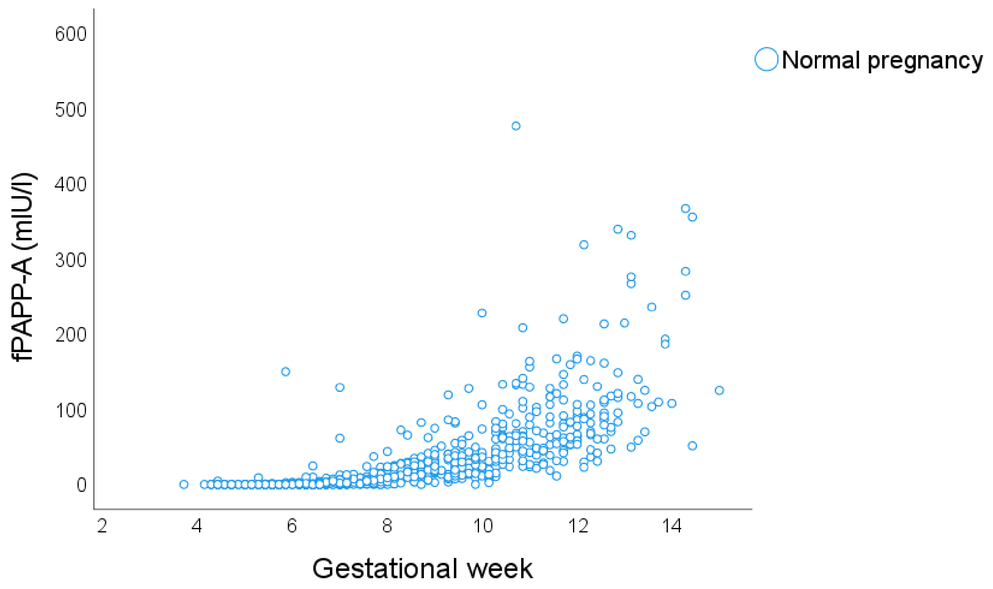


Fig 2. Scatter plot of fPAPP-A concentration against gestational age for normal pregnancies in first trimester.

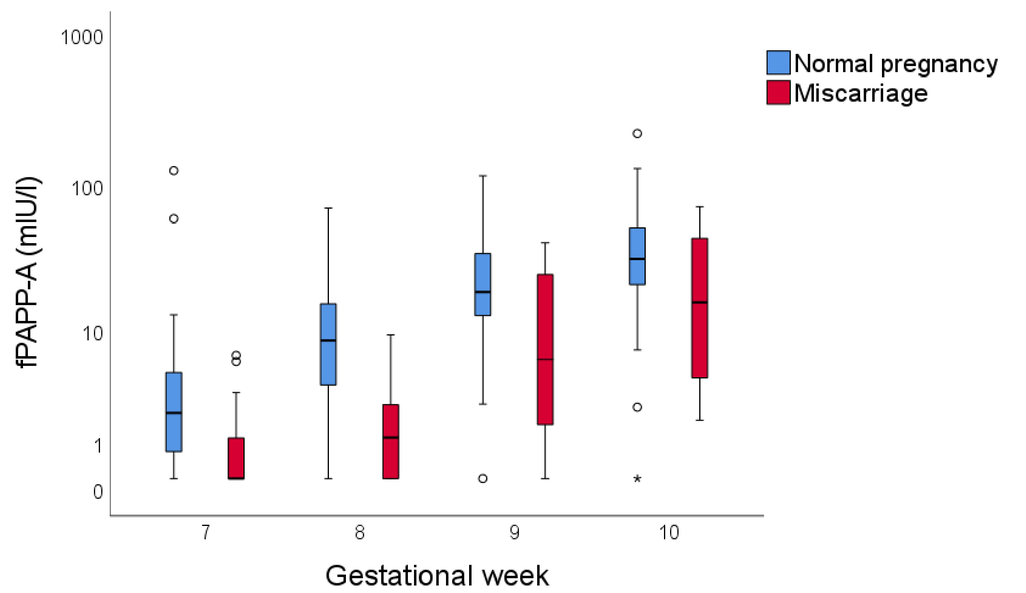


Fig 3. Distribution of fPAPP-A concentration by gestational week, separately for normal pregnancies (blue) and pregnancies ended in miscarriage (red).

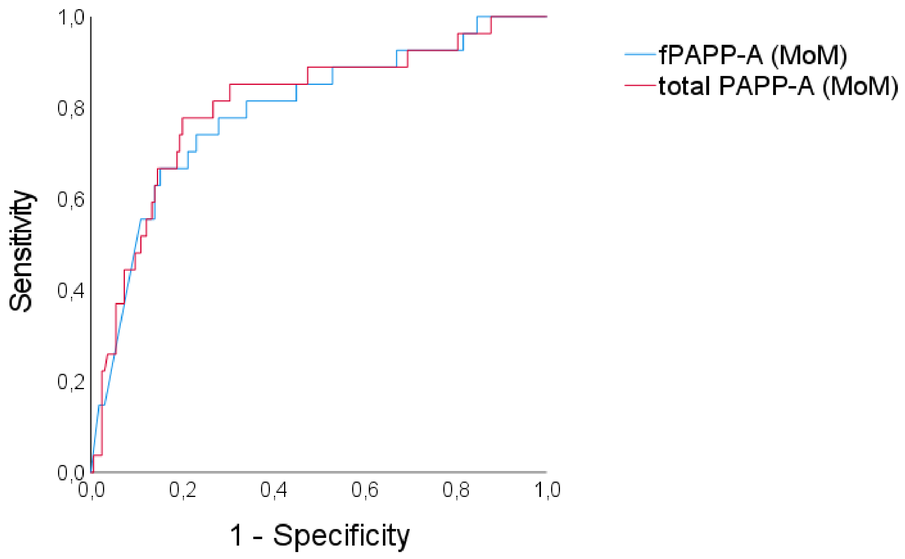


Fig 4. ROC curves for gestational week-specific multiples of median (MoM) of fPAPP-A (blue, AUC 0.79) and total PAPP-A (red, AUC 0.81) (samples of gestational weeks 7-8)

- fPAPP-A levels increased throughout the first trimester of normal pregnancy (Fig. 2).
- fPAPP-A levels were significantly lower in miscarriage pregnancies than in normal pregnancies (Fig. 3.)
- There was a strong correlation between fPAPP-A and total PAPP-A in normal and miscarriage pregnancies (Spearman's r 0.95 and 0.83, respectively). fPAPP-A was able to identify miscarriage pregnancies reasonably well but not any better than total PAPP-A (Fig. 4).

**The results suggest that fPAPP-A is not a better biomarker of miscarriage than total PAPP-A.**