



# First trimester maternal serum PAPP-A and fetal growth restriction in twin pregnancies.

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## Introduction

PAPP-A is a glycoprotein produced by the placenta. Low PAPP-A levels may result from impaired placentation or placental dysfunction, leading to suboptimal availability for the regulation of growth factors essential in fetal growth and development.

In singleton pregnancies, a PAPP-A below the 5<sup>th</sup> centile, and less than 0.4 MoM is associated with fetal growth restriction and adverse outcomes such as miscarriage, low birth weight and preterm birth. Therefore, patients with a low PAPP-A at their combined screening test are offered aspirin at 75-150mg daily and serial growth scans for early detection of fetal growth restriction in the third trimester.

Despite the evidence associating low PAPP-A levels with fetal growth restriction and adverse outcomes in singletons, PAPP-A levels are not used clinically in twin pregnancies to initiate the early use of aspirin for the prevention of fetal growth restriction and pre-eclampsia, as recommended in singleton pregnancies. In this study, we investigate the association between PAPP-A levels in twin pregnancies and fetal growth restriction.

## Results

The study included 962 women with a twin pregnancy. In the growth restricted group compared to the unaffected group, a low PAPP-A of 1.2 MoM was associated with at least one twin having birthweight (BW) less than the 10th percentile ( $p < 0.001$ ). Low PAPP-A was also associated with a BW discrepancy of more than 25% ( $p=0.001$ ) between twins. There was a significantly increased likelihood of one or both twins to be admitted to the neonatal unit ( $p=0.007$ ).

## Aim

To examine the relationship between low maternal serum pregnancy associated plasma protein-A (PAPP-A) levels and fetal growth restriction or significant inter-twin birthweight discrepancy in twin pregnancies.

## Methods

This was a retrospective study from February 2012 to June 2021. Maternal serum PAPP-A levels from twin pregnancies were measured between 11+0 to 13+6 weeks gestation and expressed in multiple of the median (MoM). Pregnancy complications and birthweight were obtained from the Hospital database. Fetal growth restriction was defined BW < 10th percentile of at least one twin. Large inter-twin BW discrepancy was defined as BW difference of at least 25% between the twins. A low PAPP-A was defined as a PAPP-A less than the 10th centile in the study population.

## Conclusions

Low maternal serum PAPP-A levels in the first trimester of pregnancy are associated with an increased risk of fetal growth restriction and adverse outcomes in twin pregnancies.

In twin pregnancies with low PAPP-A, we recommend daily aspirin as well as increased surveillance from 32 weeks gestation, for the earlier detection of fetal growth restriction, which may lead to improved neonatal outcomes.