# Association Between First And Second Trimester Maternal Screening Biochemistry, Ultrasound, And Fetal Brain Growth In Presence Of Fetal Or Maternal Congenital Heart Disease.

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## Introduction

Newer research has highlighted significant neurological impairments in children and adults with congenital heart disease (CHD). Pregnancies complicated by fetal or maternal CHD also carry a higher risk of placental abnormalities. We hypothesized that placental dysfunction in pregnancies with fetal or maternal CHD alters pregnancy hormonal levels affecting fetal brain and somatic growth.

## Methods and Materials

- We performed a retrospective case-control study on pregnant women (year 2010-2019) at the University of Iowa
- Pregnancies included were either:
  - Healthy controls (n=36)
  - Women with CHD (MCHD; n=26)
  - Fetus with CHD (FCHD; n=23)
- Only women with first and/or second trimester prenatal screening (ultrasound and blood test) were included.
- Pregnancies with fetal chromosomal abnormalities, multiple gestation, maternal diabetes, smoking, or hypertension were excluded.
- Pregnancy hormonal levels, ultrasound findings, and fetal/neonatal growth percentiles and/or z-scores data were analyzed.
- Hormonal levels were expressed at multiple of the medians (MoM).
- Fetal growth percentiles and z-scores were calculated using 2013 Fenton preterm growth chart.

## Results

| | | Controls; N=36 Mean±SD | Maternal CHD; N=26 Mean±SD | | Fetal CHD; N=23 Mean±SD | | |
|---|---|---|---|---|---|---|---|
| | | | | Vs Ctrls | | Vs Ctrls | Vs MCHD |
| **Weight** | **percentile** | 45.6±26.0 | 44.6±27.2 | p=0.90 | 28±26.8 | **p=0.02** | **p=0.05** |
| | **z-score** | -0.2±0.9 | -0.2±0.8 | p=0.93 | -0.8±1.1 | **p=0.02** | **p=0.04** |
| **Height** | **percentile** | 55.7±28.0 | 54.8±23.0 | p=0.90 | 37.7±26.7 | **p=0.02** | **p=0.04** |
| | **z-score** | 0.2±1.0 | 0.2±0.7 | p=0.99 | -0.5±1.0 | **p=0.02** | **p=0.02** |
| **Head circumference** | **percentile** | 54.7±27.8 | 46.6±29.2 | p=0.33 | 35.9±30.0 | **P=0.03** | p=0.25 |
| | **z-score** | 0.1±0.9 | 0.01±1.2 | p=0.67 | -0.5±1.3 | **p=0.03** | p=0.15 |
| **Gestational age at birth (weeks')** | | 39.3±1.2 | 38.3±2.0 | **p=0.02** | 37.8±3.5 | **p=0.02** | p=0.57 |
| **Pregnancy Associated Plasma Protein-A (PAPP-A) (MoM)** | | 1.09±0.5 | 0.9±0.5 | p=0.11 | 0.78±0.32 | **p=0.04** | p=0.60 |
| **Fetal nuchal translucency (mm)** | | 0.9±0.2 | 1.1±0.2 | **p=0.003** | 0.9±0.19 | p=0.72 | p=0.08 |
| **Expected Maternal age at delivery (years)** | | 29.5±4.5 | 25.7±4.9 | **p=0.004** | 28.4±3.2 | p=0.39 | p=0.05 |

- The control group had a positive correlation between human chorionic gonadotropin level and head circumference z-score at birth (r=0.34; p=0.053)

## Discussion

- Low PAPP-A levels early in pregnancies with fetal CHD suggests placental dysfunction reinforcing the concept of heart-placenta axis during early embryogenesis. Low PAPP-A might be associated with low insulin-like growth factor-1 (IGF-1) levels resulting in poor fetal brain growth.
- Fetal CHD group had significantly smaller height and weight percentile and z-scores compared to controls and MCHD groups. However, only fetal CHD group had significantly smaller head circumference at birth. This finding supports our hypothesis that there is an association of placental dysfunction in pregnancies with fetal CHD and brain development.

## Conclusions

- Pregnant women with CHD have increased fetal nuchal translucency and deliver at earlier gestational age.
- Women with fetal CHD have smaller neonatal brain and body size at birth with associated low PAPP-A level early in their pregnancy probably related to placental dysfunction.