

Assessment of abnormal serum analytes in low-risk patients for the prevention of adverse pregnancy outcomes

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BACKGROUND

Aneuploidy screening should be offered to all women in pregnancy.

One option of aneuploidy screening is first trimester screening (FTS), to determine the risk of trisomy 21 and trisomy 18^{1,2}.

- FTS includes placentally derived serum plasma protein-A (PAPP-A) and free beta human chorionic gonadotropin (fβhCG) between 11 and 13+6/7 weeks gestation along with an ultrasound for nuchal translucency.
 - The results of serum analytes, when combined with nuchal translucency and maternal age, produce a patient-specific risk².
 - Low levels of PAPP-A or fβhCG may indicate increased risk of chromosomal abnormalities and adverse pregnancy outcomes related to placental function.
 - » These include spontaneous abortion, preterm birth, small for gestational age (SGA; birth weight less than 10th percentile), preeclampsia, and stillbirth (fetal death prior to delivery after 20 weeks gestation or where the products of conception weights at least 500 grams)³⁻⁶.

Literature varies as to the serum analytes studied and the cut-offs used to identify adverse pregnancy outcomes^{4,5,7,8}.

- Many failed to utilize low fβhCG or a combination of PAPP-A and fβhCG outside of the normal range.
 - The 2017 SOGC update on prenatal screening for fetal aneuploidy, fetal anomalies, and adverse pregnancy outcomes states that universal screening for adverse pregnancy outcomes using maternal serum markers is not recommended².

In Canada, SGA is evident in 8% of births⁹, preterm birth complicates 7.8% of live births¹⁰, preeclampsia is present in 4.5%¹¹ and the rate of stillbirth is 0.45 – 0.73%^{12,13}.

There is evidence that aspirin use in pregnancy, when initiated at < 16 weeks gestational age, can minimize placentally-related adverse pregnancy outcomes¹⁴.

There is associated morbidity and mortality for both the pregnant women and neonate and should continue to be investigated to be minimized.

Hypothesis: We predict that normal aneuploidy screening does not preclude a diagnosis of an adverse pregnancy outcome and instead, if interpreted early, can help guide management in pregnancy.

OBJECTIVES

1. To identify women at a Canadian centre who screened low-risk for trisomy 21 and 18 on first trimester screening (FTS), had a normal karyotype and/or cell free DNA result and had serum analytes matching a combination of PAPP-A < 0.3MoM and fβhCG < 0.5MoM or > 2.5MoM
2. To determine the occurrence rate of individual and composite adverse pregnancy outcomes in this population, including preterm birth, small for gestational age (SGA), preeclampsia, and stillbirth
3. To determine the occurrence rate of composite adverse neonatal outcomes in this population, including NICU admission, cord pH < 7.0, Apgar at 5 min < 7, and/or any other neonatal concern documented by a healthcare professional

METHODS

Type of Study: Retrospective chart review

Population: Pregnant women who completed first trimester screening (FTS) for fetal aneuploidy

Location: Regina, SK, Canada

Dates: January 1, 2010 and December 31, 2019

Inclusion Criteria:

- Screened low-risk for trisomy 21 and 18, had a normal karyotype and/or cell free DNA result
- Serum analytes plasma protein-A (PAPP-A) < 0.3 MoM and free beta human chorionic gonadotropin (fβhCG) < 0.5 MoM or > 2.5 MoM

**All other patient results from the aneuploidy database were excluded*

Data Collected:

- Age
- BMI at < 20 weeks gestation or the time of scheduling FTS
- Gravidity
- Parity
- Number of fetuses
- Medical comorbidities
- Smoking status
- Substance use
- Aspirin use
- Gestational age at delivery
- Route of delivery
- Infant gender(s)
- Birthweight **converted to percentiles*
- Cord pH
- Apgar scores
- Neonatal concerns

Analysis:

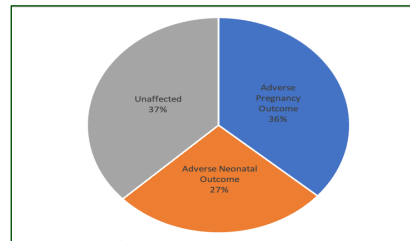
- Mean age
- Mean BMI
- Spontaneous abortion **excluded from further analysis*
- Adverse pregnancy outcomes – individual and composite rates
- Adverse neonatal outcomes – composite rate

RESULTS

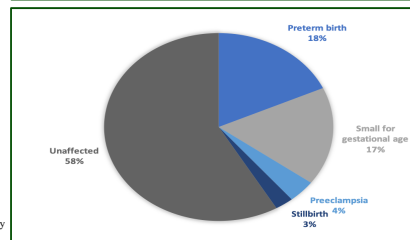
Mean age: 28.6 ± 5.2 years

Mean BMI: 28.5 ± 7.1

Composite Adverse Outcomes:



Individual Adverse Pregnancy Outcomes:



* Spontaneous abortion occurred in 23.3%
* 2 patients were started on aspirin in pregnancy

CONCLUSIONS

- Aneuploidy screening should continue to be offered to all women in pregnancy.
- Placental serum analytes (PAPP-A and fβhCG) contain valuable information for all providers of obstetrical care.
- Adverse pregnancy and/or neonatal outcomes may be seen in patients with low-risk aneuploidy screening.
- The findings support the need for universal risk-based screening of all women in pregnancy.
- Obstetrical providers should guide management according to risk.
- Consideration for aspirin use in those with normal aneuploidy screening but abnormal serum analytes may help minimize placental-related adverse pregnancy outcomes.
- Appropriate obstetrical care, monitoring and timely delivery is imperative to decrease morbidity and mortality.

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