

Prediction of stillbirth by first and second trimester biomarkers

Abstract

Stillbirth is one of the most common and devastating experiences for pregnant women and their obstetricians; predicting stillbirth will not only allow us to monitor these women and their fetuses more closely, but also helps in preventing them from its occurring. First and second trimester biomarkers can be used for this purpose. Though abnormal values of these tests have a significant relationship with future stillbirth risk, the low positive predictive value and sensitivity hinders their use as a screening tool.

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Introduction

Stillbirth affects 1:200 pregnancies and is one of the most common complications of pregnancy;¹ experiencing a stillbirth is a devastating experience for a pregnant woman, her family as well the obstetrician who cares for her. Once there is a stillbirth, there is little that can be done to alleviate the sorrow and guilt that the parents and doctors go through.^{2,3} Thus finding ways to predict and prevent stillbirth would be one of the most important areas in new developments in modern fetal medicine. A stillbirth can be defined as a fetal death after 22 weeks of gestation or when the gestation is unknown a fetal weight more than 500g at the time of delivery.¹ Screening for risk of stillbirth should be carried out from the first perinatal visit and continue throughout pregnancy. Risk factor identification from history, biochemical tests and ultrasonography can be used for this purpose.

Abnormal placentation is responsible for most of the unexpected stillbirths.⁴ These include the stillbirths occurring due to pre-eclampsia, fetal growth restriction and placental abruption and as placenta secretes many proteins in maternal serum, analyzing them might give clues about abnormal placental function.¹ As Down syndrome screening using serum markers are widely available now a days, using these markers to predict stillbirth can be evaluated more widely. The first trimester serum biomarkers like pregnancy associated plasma protein A (PAPP-A) and free beta human chorionic gonadotrophin (Free β hCG) and second trimester biomarkers like alpha fetoprotein (AFP), unconjugated Oestriol (uE3), hCG and inhibin A has been evaluated in this regard.⁵

PAPP-A

This is a protease that is secreted by the syncytiotrophoblast and when its value in first trimester is less than the 5% of normal, the risk of stillbirth increase up to 50 folds.⁶ The risk of stillbirth increases when the level of PAPP-A becomes lower. In spite of statistically significant differences, the sensitivity and positive predictive (PPV) for PAPP-A is low.⁵

Free β hCG

This is also synthesized from syncytiotrophoblast and its low

levels in first trimester is associated with early stillbirth (<24weeks). But there is evidence about the risk of stillbirth in fetuses more than 24weeks with low levels of serum free β hCG is conflicting.⁷

AFP

This is oncofetal protein and a low or high level of this protein is associated with adverse fetal outcome and stillbirth.⁵

uE3

A low level of uE3 less than the 0.5MoM is associated with fetal growth restriction and early fetal loss.⁸

Inhibin A

Initially is produced by the corpus luteum and then by the placenta. This is a protein which is initially produced by the corpus luteum and then by the placenta. It has a role in cell differentiation and growth.⁵ Increased levels of inhibin-A in second trimester is found to be associated with poor obstetric outcomes including stillbirth.⁸

Conclusion

Though there is promising results in favor of adverse pregnancy outcome prediction with abnormal biomarker levels, the problem is in isolation and even in combination these serum biomarkers have low sensitivity and PPV to be used as screening test to predict stillbirth.⁵ Future directions would be combination of maternal risk factors and ultrasonography with these serum biomarkers to produce composite scores to help predict stillbirth and adverse pregnancy outcome. When there is a risk of stillbirth the only method of preventing it is early delivery, thus it is very important that decision to deliver should be taken very carefully in order to prevent unnecessary iatrogenic prematurity. The way forward would be to find ways to predict stillbirth more accurately thus we can prevent it from happening without the excess risk of iatrogenic prematurity and its complications.

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Conflict of interest

The author declares no conflict of interest.

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