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Prematurity: Still A Challenging Problem

Prematurity remains one of the most common problems that we deal with in obstetrics and pediatrics. The overall number of preterm births has decreased slightly to approximately 9.6% in 2014. The prior increase was due to an increase in late preterm births from 34 weeks to 36-6/7 weeks gestation, accounting for the fastest growing subset of neonates, which accounted for 74% of all preterm births and fell from 9.1% to 8% between 2006 and 2013. The very preterm birth rate has been fairly stable since 1990. The recent overall decline is likely attributed to a decrease in the late preterm births, 70% of which are spontaneous. The March of Dimes released their annual report card in October 2015 on the 2014 preterm birth rate. The rate continues to decline, although the United States ranks 26th in 29 developed countries in infant mortality. The US received a grade of C and Georgia received a grade of D (rate between 10.4 and 11.4%) in terms of preterm birth rate from the March of Dimes.

This trend seems to be attributable to increasing use of early ultrasound dating, preterm induction and preterm cesarean delivery without labor and changes in social demographic and behavioral

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factors. Preterm births for patients delivered by cesarean, induced vaginal birth and non-induced vaginal birth have all declined.

The mortality of infants born before 24 weeks is high. The survival rate increases dramatically between 24 and 25 weeks. National newborn survival has increased. 30-32% of 22 and 23 week deliveries survive. Approximately 50% of 24-week delivery survive. 75% of 25 week deliveries survive.

In addition to being the leading cause of neonatal mortality (particularly in infants born less than 32 weeks) in the US, preterm birth is the primary cause of neonatal morbidity, including infectious and noninfectious respiratory, gastrointestinal, immune system, central nervous system, hearing, and vision issues. Preterm birth is also associated with long-term adverse outcomes such as neurodevelopmental disabilities including cerebral palsy cognitive impairment, altered lung function, metabolic and cardiovascular risk, decreased long-term survival and reproduction.

Average first year medical costs in 2005 were \$33,200 for a premature infant. Adjusted for inflation this is approximately \$46,000 in 2015 dollars. Preterm birth is routinely associated with longer neonatal hospital stays, rehospitalizations, extended time in the neonatal intensive care unit. These costs are approximately 10 times that of a normal term newborn.

Preterm labor is likely one syndrome with many causes. Spontaneous preterm birth leads to 70% of preterm births. These potential causes include infection, hemorrhage, uterine overdistention, and activation of the maternal/fetal hypothalamic pituitary axis. These pathways converge on a final

common pathway that involves myometrial activation and cervical change and/or PROM.

Multiple risk factors are associated with spontaneous preterm birth including. These include history of spontaneous preterm birth, multiple gestation, cervical insufficiency, uterine abnormalities, vaginal bleeding, anemia, low prepregnancy weight, and infection. Additional factors include African-American ethnicity, maternal age less than 17 and greater than 35 years, low social economic status, maternal stress, and behavior patterns such as cigarette smoking and drug abuse. However more than half of women who deliver preterm did not have identifiable risk factors and two thirds of women with risk factors go on to deliver at term.

Symptoms of preterm labor may increase the likelihood of PTD. However, among those who present in preterm labor, 30% will spontaneously resolve, and 50% of those who are hospitalized will give birth at term. Less than 10% of women with a clinical diagnosis of preterm labor actually give birth within 7 days of presentation. Contractions alone are a poor predictor of preterm delivery.

Evaluation of fetal fibronectin and transvaginal ultrasound for cervical length may be helpful in predicting risk of preterm delivery in those who present with symptoms of preterm labor. Fetal fibronectin is a component of the extracellular matrix of the membranes of the amniotic sac. It is found in the interface between the chorion and decidua. It is an adhesive or "biological glue" that binds the fetal sac to the uterine lining. It is typically absent from cervicovaginal secretions from 24 weeks until near-term. When it is present there may be an increase likelihood of preterm delivery.

Likewise, cervical length by transvaginal ultrasound can be a predictor of likelihood of preterm delivery. If cervical length is greater than 30 mm and or fetal fibronectin is negative risk of preterm delivery is low and the patient may be managed accordingly.

Conversely in the presence of cervical shortening (e.g. <20 mm but it varies from study to study) and or positive fetal fibronectin, steps can be taken to prepare for possible preterm delivery such as transfer to a tertiary care center, antenatal corticosteroids, magnesium sulfate for fetal neuroprotection if less than 32 weeks, and tocolytics.

Antenatal corticosteroids between 24 and 34 weeks may reduce the risk of neonatal death, RDS, IVH, cerebroventricular hemorrhage, NEC, NICU admissions, and early systemic infections. A recent trial suggested antenatal corticosteroids may be helpful in the late preterm group if they are at risk for delivering before 37 weeks' gestation, are nondiabetic, and have not received a previous course of antenatal corticosteroids. These newborns have been shown to have a lower risk of neonatal morbidities such as respiratory issues. Antenatal corticosteroids are most effective if administered more than 24 hours and within 7 days of preterm delivery.

Standardization of practice in hospitals may improve outcomes in patients who are at risk for preterm delivery. Standardization can also reduce cost when protocols are in place and used effectively. The March of Dimes has a preterm labor assessment tool that can be used for evaluation of patients who presented in preterm labor.

If you have further interest I will be speaking about preterm labor and assessment at the conference in September.

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