Preterm birth: a global burden on maternal and child health

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Introduction

A report released May 2, 2012 by the United Nations Secretary General, Ban Ki-moon, reported a global crisis in the rising rates of preterm birth (<37 weeks gestational age) and prematurity due to low birth weight (<2500 grams). 'Born Too Soon: The Global Action Report on Preterm Birth' features the first-ever estimates of preterm birth rates by country.¹ Authored by a broad group of 45 international multi-disciplinary experts from over 26 organizations and 11 countries, this report is written in support of all families who have been touched by preterm birth. The report highlights the following:

- 15 million babies are born too soon every year and more than one in 10 babies are born preterm, affecting families all around the world;
- over one million children die each year due to complications of preterm birth. Many survivors face a lifetime of disability, including learning disabilities, and visual and hearing problems;
- preterm birth rates are increasing in almost all countries with reliable data;
- prematurity is the leading cause of newborn deaths (babies in the first 4 weeks of life) and now the second leading cause of death after pneumonia in children under the age of 5;
- global progress for child survival and health to 2015 and beyond cannot be achieved without addressing preterm birth;
- investment in women's and maternal health and care at birth will reduce stillbirth rates and improve outcomes for women and newborn babies, especially those who are premature.¹

Although the burden of preterm birth extends globally, its impact dominates in the USA, Africa, and Southeast Asia. Recent estimates from the World Health Organization (WHO) indicate that ~12.5% of births in these regions are preterm; however, actual rates in Africa and Asia are expected to be much higher.² The primary goal of the 'Born Too Soon' report is to generate discussion in various social and

political forums, and create awareness among politicians, as well as developing strategies to prevent preterm birth at the local, regional, and global level. Increasing understanding about the knowledge gap between preterm birth research and clinical interventions is one of the major objectives of the report; some remedial strategies are described below.

Complexities of a complex problem

Preterm birth is a complex syndrome,³ and it is complicated by heterogeneities in every facet of its understanding. The unraveling of the complexity of preterm birth should start with proper definition of pregnancy outcome.⁴⁻⁷ Preterm birth is commonly classified into three categories: 1) 'medically indicated (iatrogenic)' (accounting for 25%; 95% CI=18.7–35.2%), 'spontaneous (idiopathic)' preterm birth (PTB) (50%; 95% CI=23.2–64.1%) and 'preterm premature rupture of membranes (pPROM)' (25%; 95% CI=7.1–51.2%). Failure to provide proper definitions in study designs and the mixing of multiple outcome phenotypes have hampered proper understanding of etiologies and pathophysiologies.²⁻⁶ Attempts have been made to highlight the significance of this problem and recent initiatives are expected to improve this issue. The rates of preterm birth are relatively stable in the developed world, ranging from 5% to 10% according to the social and nutritional status of the mothers. It should be taken into account that many subgroups of preterm births are iatrogenic because of maternal illness or developing fetal compromise.

Generalization of risk and risk associated pathophysiology

Failure to reduce the preterm birth rate can be partially blamed on generalization of this condition worldwide. There is a major disconnection between various branches of research and intervention when it comes to filling the knowledge gaps. Epidemiologic and environmental risks are not always global; risk assessment should be carried out progressively at local, regional, and then global levels. The risk-induced

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pathophysiologic pathways resulting in preterm birth may also vary based on differences among various factors including, but not limited to, geographic origin, racial/ethnicity, social, biodemographic variations and environment, cultural, religious and behavioral factors, access to care, infections agents and environmental toxicants, genetic and epigenetic factors, etc.⁸ Manifestation of preterm birth risk in an individual can differ based on so many factors, and the pathophysiologic pathways and biomolecular factors associated with adverse pregnancy outcome is likely to be different (pathophysiologic heterogeneities) in a given pregnant subject from a given location. This is further complicated by complex interactions between various factors like environment $\times$ environment, gene $\times$ environment, and gene $\times$ gene. The type of interaction and its manifestation in a given individual will be different, and understanding of such factors is essential for tailored intervention.⁸ Therefore, generalization of risk, risk-associated pathways, and interventions without the knowledge of underlying causality are all likely factors creating failure in our current approaches to prevent preterm birth.

Need for personalized medicine to reduce the risk of preterm birth

Based on our current knowledge, interventions are aimed at preventing terminal events resulting in preterm birth where a provider will not have the opportunity to assess risk and provide appropriate intervention based on individual's own risk factors or risk associated pathways and biomarkers. Filling the knowledge gap of the risk assessment system and tailoring prevention management based on specific risks at local, regional, and global level is essential to providing personalized care that can reduce the burden of preterm birth for a pregnant subject. Universal intervention approaches have failed, and it is time to consider assessing risks at each individual level and tailoring the intervention to the mother's 'own' factors that are contributing to adverse outcome. This prevention program should start early in pregnancy based on risk factors that are static and will not change during the course of pregnancy. Interaction of risk factors with pregnancy-associated environment may change and manifestations may differ in a given individual. Monitoring these changes and personalizing interventions are likely solutions for reducing the rates of preterm birth.

Action is needed where activity is the most

Most of the studies aimed at understanding the complexity of preterm birth risk have been, to date, limited to developed regions (North America, Western Europe, and Australia). Very few in depth studies have been conducted in areas where maternal, fetal, and neonatal mortalities due to preterm labor and preterm birth are high, e.g., Africa and South Asia. As mentioned, the risk factors are not universal and their manifestations are not the same in all subjects. Therefore, more coordinated research is needed to understand risk factors in regions where preterm birth risks are very high.

Lack of research funding, over decades, towards understanding the causality and design intervention strategies to prevent preterm birth has hurt our chances to move forward. To improve global pregnancy outcome and reduce maternal and neonatal mortality global, attention should be diverted to more funding and support of the research and clinical community. Reducing the preterm birth rate is achievable; a coordinated action between various agencies and health providers and researchers, early identification of high risk subjects for preterm labor, tailoring preterm labor interventions based on a subject's own risk factors, and educating the public on causes and short- and long-term consequences of preterm birth are essential to achieve global progress for child survival and health to 2015 and beyond.¹

References

- 1 World Health Organization; March of Dimes; The Partnership for Maternal, Newborn & Child Health; Save the Children, *et al.* Born too soon: the global action report on preterm birth. Available at http://www.who.int/pmnch/media/news/2012/preterm_birth_report/en/index.html
- 2 Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Harris Requejo J, *et al.* The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bull World Health Organ.* 2010;88:31–8.
- 3 Romero R, Espinoza J, Kusanovic JP, Gotsch F, Hassan S, Erez O, *et al.* The preterm parturition syndrome. *BJOG.* 2006;113(Suppl 3):17–42.
- 4 Villar J, Papageorghiou AT, Knight HE, Gravett MG, Iams J, Waller SA, *et al.* The preterm birth syndrome: a prototype phenotypic classification. *Am J Obstet Gynecol.* 2012;206:119–23.
- 5 Goldenberg RL, Gravett MG, Iams J, Papageorghiou AT, Waller SA, Kramer M, *et al.* The preterm birth syndrome: issues to consider in creating a classification system. *Am J Obstet Gynecol.* 2012;206:113–8.
- 6 Kramer MS, Papageorghiou A, Culhane J, Bhutta Z, Goldenberg RL, Gravett M, *et al.* Challenges in defining and classifying the preterm birth syndrome. *Am J Obstet Gynecol.* 2012;206:108–12.
- 7 Ananth CV, Vintzileos AM. Epidemiology of preterm birth and its clinical subtypes. *J Matern Fetal Neonatal Med.* 2006;19:773–82.
- 8 Menon R. Spontaneous preterm birth, a clinical dilemma: etiologic, pathophysiologic and genetic heterogeneities and racial disparity. *Acta Obstet Gynecol Scand.* 2008;87:590–600.