

## The challenges and unresolved dilemmas of prematurity

Preterm birth is one of the most serious problems that still persists in health care and which apparently will not improve over the next years.

Having this in mind could help us understand and accept the limitations of medicine in relation to conditions that respond to factors that cannot be corrected under the current scope.

The concept of health exceeds the limits of medicine because it involves multiple aspects of everyday life. Believing that medicine is exclusively responsible for ruling subjects' health and preventing disease is a fallacy of these times, when medicalization has pervaded even the most unusual facets of people's lives. Nowadays, people are more and more dependant on health care, but they do not understand that health is part of a complex and multifactorial process. This does not undermine all the achievements accomplished in the field of medicine in terms of health improvement and disease prevention. A clear example of this are vaccines, which have certainly helped to make many severe diseases fade away. However, for vaccines to be successful, individuals should get vaccinated. Although it may sound obvious, many people in the world have no access to vaccines and, therefore, their benefits depend on multiple factors that lie beyond the scope of medicine. Looking at the history of humankind, countless examples can be found of improved life conditions that were closely related to health. Just to mention an example, almost 2500 years ago Romans built aqueducts that carried drinking water for centuries, which are now considered the biggest and most significant engineering works of the ancient world in relation to sanitation.

Today, in the 21<sup>st</sup> Century, preterm births are still one of the most pressing, unsolved problems facing public health. Premature infants account for approximately 40% of deaths in the first year of life, with newborn infants with a birth weight less than 1500 g having a relative risk of death 200 times higher and accounting for 50% of neonatal mortality, although they constitute only between 1% and 2% of all births.

The major concern today is that the prematurity rate is far from decreasing in many countries; in fact, it has stabilized and has generally steadily increased for the past 20 years across the world.

It may seem paradoxical that in an era characterized by huge advances, prematurity is still a real challenge for the so-called "powerful" mod-

ern medicine. In USA, prematurity accounts for more than 12% of all live newborn infants, a 20% increase from 1990. The same trend has been observed in most high income countries, including Eastern Europe countries, Japan, Australia and Canada, even when rates are lower. As an example of the extent of this problem, USA currently ranks 131 out of 184 countries worldwide in the prematurity rate ranking. What is the explanation for this? Is it possible to have an increased prematurity rate, similar to that observed in many low income and low resource settings, in a country that has made the most contributions to research and medical advances?

This scenario points out the challenges and problems of prematurity. One of these depends only partially on medicine, the other falls entirely under the responsibility of the medical field, particularly the care provided at neonatal intensive care units (NICU) to premature infants born in the limits of viability.

As demonstrated, the first of these approaches is related to health and is mainly originated in the living conditions of individuals, the effectiveness of measures taken by governments, the education and culture and, to a lesser extent, medicine; the second approach originates in medical ethical principles. Both approaches are highly complex and different. I will describe only the most relevant aspects of each one.

The study of human physiology is based on the assumption that births occur at 40 weeks of gestation, with little variation. Yet, it has not been possible to certainly establish if preterm birth mechanisms are equal to those of term births and only take place earlier than expected, or if a preterm birth actually triggers different mechanisms.

Several studies have demonstrated that social factors, including poverty, scarce maternal education, adolescent pregnancy, single motherhood, alcohol use, smoking, etc., substantially increase the risk of prematurity. In addition, these social, economic and cultural determinants account for maternal biologic factors, such as low weight and height, and/or a poor nutritional status during pregnancy, which are also associated with a higher risk of prematurity.

The mother's ethnicity is also a consistent risk factor. In USA, the prematurity rate in the African-American population doubles that of Caucasians, and recurrent preterm births are four times more

common among African-American mothers; these differences persist even after controlling confounding factors. The reasons for this are still unclear. An explanation has been sought in genes, but no genetic variation among ethnic origins has been demonstrated. Another aspect of much interest is the "social stress" caused by a long history of discrimination against the African-American population in USA, which constitutes a significant risk factor. This is supported by several studies that also found that the prematurity rate among African-American mothers born in USA was even higher than the one observed among African-American mothers born in a different country, and the risk of experiencing adverse pregnancy events was even 40% higher among the African-American mothers born in USA compared to their own mothers and grandmothers born in Africa or the Caribbean ("*The enigma of spontaneous preterm birth*"; *NEJM* 2010;362:529-35)

This example, and certainly others that have not been identified or made clear yet, could explain why social support strategies during pregnancy have not been effective for the reduction of prematurity rates. Social problems and poor living conditions exist before pregnancy and require very profound approaches to be improved.

The medical approach to prematurity has mainly focused on treating its consequences instead of preventing them. Multiple obstetric measures based on risk factors have been taken, including antibiotics for uterine inhibition, cervical cerclage, bed rest, reduced working hours, but they have all failed. Progesterone therapy seems promising to reduce recurrence in mothers with a prior preterm birth, but more robust evidence is still required.

It is also true that medicine itself has contributed to increasing the rate of prematurity over the past 20 years. The most remarkable examples are the sharp increase in the number of unnecessary caesarean sections (iatrogenic causes) before reaching 37 weeks of gestation and the high number of multiple pregnancies due to medically-assisted fertilization.

To sum up, we could state that a perinatal approach to prematurity has mainly focused on care

provided at the NICU. This has led to much progress but at the same time it has resulted in several unfavorable aspects related to ethical matters in terms of the survival rate of extremely small preterm infants, which has increased in most neonatal units especially from the 90s

A bioethical approach to newborn infants within the limits of viability deals with looking for a balance between acceptable and unacceptable risks, which is hard to attain if we do not take into account that not all that can be done should be done. Actually, the initial progress of these infants raises more questions than certainties, but irreparable consequences are usually identified over the first few days or weeks. Therefore, it is fundamental to reflect on our actions and share our doubts and worries with other health care professionals in order to ascertain what works best for patients and their families. Giving parents clear information and making them become actively involved is essential for the entire process, but when times are critical, it is common to realize that doctors have more power than parents. The course should shift to considering parents as "partners" of doctors, and then both can be considered to be on more equal terms. A bioethical reasoning regarding which measures to take when infants have an unavoidable unfavorable prognosis and irreversible damage should be based on consensus between parents and physicians.

Finally, I would like to highlight that the challenges posed by prematurity in relation to prevention will not change in the short term, and we will continue to be forced to live with this sad situation. But this should not leave us powerless; on the contrary, we should acknowledge that we need to have an honest approach to ethical dilemmas associated with extremely premature infants and reinforce our actions by actively becoming involved in their care and helping those who suffer prematurity. ■

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