



Editorial

New aspects on prematurity

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Prematurity is one of the most prevalent health problems in children of developed countries. Between 8 and 10.5% of births take place before 37 weeks of gestation and justify 75% of perinatal mortality and 50% of disability in infancy. In this number of *Evidencias en Pediatría* the excellent article published in *JAMA* in March 2008 is critically appraised^{1,2}. In this study new information is exposed on the long term effects of prematurity. For this purpose information has been obtained on all the cohort of newborn children in Norway between 1967 and 1988. The authors conclude that prematurity is associated with an important reduction of long term survival, a limitation of reproductive capacity and that the women that were themselves premature had a higher risk of having premature children.

Neonatologists were basically concerned with the survival of premature children. But it was soon obvious that the mortality in premature children was only one part of the picture. Risks of cerebral paralysis, blindness, mental retardation and deafness were clearly higher in premature children when compared with those of children born at term^{3,4}.

More recently, as follow up of very premature children has continued through school age, it has been proven that even those that at age 2 years were considered normal, without any type of limitation, had lower academic performance due to difficulties in learning, attention problems, visual-motor coordination, emotional problems and social integration⁵⁻⁹. The professional teams that are responsible for the follow up of these "new morbidities" are still looking for the adequate instruments for early diagnosis and the effective interventions to improve academic performance and social competence. This has also had an impact on the work of Neonatal Units that are now paying special attention to other type of methods of care, centered in development, that are not so centered in the treatment of disease as in the adequate neurological and emotional development of the child¹⁰. The access of parents to the Neonatal Units has become much less restricted as a means to involve parents in the care of their child and favour bonding, and on the other hand care is taken to avoid stressors from the environment, reducing aggressive stimuli and preventing and treating with exquisite attention any pain so as to allow the central nervous system of these very immature children to adequately develop out of the mother's uterus¹¹.

In the meantime, while we are trying to understand and prevent all these cognitive, attention and behavioural problems of premature children, Swamy et al¹ open a new perspective in relation to other aspects that until now have not been addressed (or had been addressed

in a much more limited way), including providing proof that prematurity in one generation of women influences prematurity in the next generation.

All this being said, we have to address another series of circumstances that make prematurity one of the most important health problems in the developed countries, but for not well known reasons, has less visibility than other diseases.

Even though great efforts are being made in clinical practice and research, the frequency of prematurity in developed countries is increasing. It was believed that with the establishment of obstetric controls for all the population the number of premature births would diminish, but this has not been the case. In the United States premature births have increased from 9.5% in 1981 to 12.7% in the year 2005¹². It could be the case that health policy in the United States has a discriminatory effect for some sectors of the population and that this could be the underlying cause. However in Denmark and Norway, that have a universal health coverage and optimal prenatal care standards, this increase in the number of premature births has also occurred. In the year 2006 a population based study in Denmark¹³ exposed that the proportion of premature births had increased by 22% between the years 1995 and 2004. In Norway, from the year 1980 to 1998, they detected an increase 25% of the rate of prematurity¹⁴. Factors that contribute to this increase are: assisted reproduction techniques in relation to multiple gestations, and also when a single embryo is implanted¹⁵. On the other hand, better results in outcome of premature children have increased the indications for ending pregnancy, before term, in interest of the mother or the foetus. The increase in maternal age also has a higher risk of premature birth, and work conditions or stress have also been associated with a greater frequency of prematurity^{16,17}. Even taking into account all these factors does not justify the magnitude of the increase in the frequency of premature births.

As well, premature birth has been associated with numerous socioeconomic factors, including maternal level of education, employment status, and income. Two studies continue to show that these differences in prematurity in relation to socioeconomic status still persist. In the Norwegian study¹⁴, published in the year 2006, proof is provided that the rate of prematurity is greater in women that have a low educational level compared to women with higher education (odds ratio [OR]: 1.55; 95% confidence interval [CI 95%]: 1.48-1.62). This difference remains more or less stable during the whole period of the study. In the Health Area of Trent in the United Kingdom¹⁸ the frequency of births with a

gestational age inferior to 32 weeks was evaluated for the years 1994 to 2003. The frequency of very premature births was 1.64 % in the less favoured social classes against 0.85 % in the more favoured social classes (OR: 1.94; CI 95%; 1.73-2.17). Therefore, prematurity is not only globally significantly more frequent in women with less resources, but also the birth of very premature children (children with a gestational age < 32 weeks) is twice as frequent in them. If we add to this the fact that one of the determinants of the short and long term evolution of very premature children is maternal education¹⁹, we find that the most immature children are usually born in families with scarce resources and that this situation, most importantly lower maternal education is associated with a worse evolution.

The care and study of the evolution of very premature or very low birth weight (weight at birth < 1500 grams) children has been the primary objective of neonatal teams and during the last two decades, numerous studies are dedicated to the attention received by these children. However, even though births between 32 and 36 weeks of gestation are at least five times more frequent than those inferior to 32 weeks, their impact in public health is not well studied and has received scarce attention. The tendency to trivialize the problems that these children present has become evident even in the name they have received. The group of newborn children between 34 and 36 weeks of gestation has been called almost at term" bypassing their principal characteristic, that is to say: prematurity. Recently Engle et al²⁰ propose that they be called "late premature", since the term "almost at term" can condition the obstetric and neonatal care and not take into account the greater mortality and morbidity that these children have when compared to at term newborn children. These late premature children have a physiological and metabolic immaturity, and therefore, will develop medical complications that require treatment in Neonatal Units with much more frequency than those born at term. A large cohort study²¹ that had as a purpose to determine the frequency of admissions to the Neonatal Units at different gestational ages showed that premature children born at 34 weeks of gestation were admitted, 54% of those born at 35 weeks of gestation, 25 % of those born at 36 weeks, 12% of those born at 37 weeks and 2.6 % of those born between 38 and 40 weeks.

The severity of the diseases that they suffer can be deduced by the increase of mortality compared to at term children. In the year 2002 the mortality of late premature children in the United States was 4.6 times greater than of those born at term. They also have a greater frequency of readmissions and some information suggests that they have a greater risk of cerebral palsy²², language problems²³ and, conduct problems and social competence²⁴. Even though they are the most frequent premature group, the emotional, personal, and economic cost of late premature children are not sufficiently evaluated.

If we pay attention to the other extreme of prematurity, in extremely premature children (gestational age < 26

weeks), we find important ethical (part from the medical and prognostic factors) aspects that have appeared in relation to the decisions to treat or not to treat those children in the limits of viability. There is no general agreement over the precise meaning of "limit of viability", but actually the majority of authors that use this term refer to children with ages inferior to 26 weeks of gestation. In April 2008, Tyson et al²⁵ have published the results of a cohort study of 4,446 children born between 22 and 25 weeks of gestation. The 83 % of them were admitted in neonatal intensive care. At 18 months of corrected age 71% had died or had disability. Female gender, prenatal corticosteroids, single fetus and greater gestational age were favourable prognostic factors. Surprisingly female children have lower probability of receiving active treatment when these factors are taken into account. If the results of this study are taken into account, the decision to treat or not children of gestational age < to 26 weeks is still in a "grey (very gray) zone". It is difficult to justify the suffering and the emotional cost of intensive care in very premature children for the child and its family, especially if we take into account the unfavourable results in outcomes. The authors of this excellent study propose an informatic tool that allows prediction at individual level of the probabilities of good outcomes. In this way the neonatologists and the parents, could make use of an instrument that estimates in a more precise way the magnitude of the benefit that intensive care can offer for a specific child, taking into account the differences that exist in different centers.

When time comes to decide whether to treat a newborn child younger than 26 weeks of gestation, it is the usual practice in most countries to involve parents who, taking into account the principle of autonomy, as responsible for the best interests of the child, have to decide after the information given by the professional teams. Even though this is so theoretically, the parents' perception differs from that of the professional teams. Helen Harrison became a mother of a premature child in the year 1975 and since then has worked and published information on many aspects of prematurity parents, family burdens, and the information that professional teams give parents when decisions are made at the moment of treating or not. She has recently published a new work²⁶ in which she sustains that the information that is given to parents by professional teams is insufficient in relation to the consequences of prematurity, reanimation, intensive care treatment and on all the possible options. In this way, inadequately informed parents especially due to a positive bias on the outcomes take decisions of great importance for their child and for their family. She even criticizes the way in which results are presented in certain studies that have been considered "references" as for example the study on quality of life undertaken by Sargal et al²⁷. Harrison sustains that these studies induce in an unjustified manner a favourable approach to admission in intensive care units of extremely premature children.

After having analyzed in a succinct form some of the

most polemic aspects of prematurity we remain with a sense of pessimism and relative perplexity. As has been expressed at the beginning of this commentary in the year 2008 information has been published on the long term consequences of prematurity. On the other hand the frequency of prematurity is increasing and there is no perspective of any way of stopping this increase. Furthermore we have seen how prematurity in general, and very premature children in particular are more frequent in lower social classes. We also want to emphasize how limited information is on late premature children even though they are the most frequent group, and the tendency there is to trivialize their physiological and metabolic immaturity. If this was not enough we have seen how the evolution of children of gestational ages inferior to 26 weeks is very disfavoured and, in consequence there are doubts on who should be treated once the risks and benefits have been taken into account. Last, even though professional teams try to respect the autonomy of the parents, the parents perceive that the information they receive is biased and insufficient. Nevertheless, there is also "good news" in relation to prematurity. There is no doubt that survival rates unimaginable in earlier times have been achieved. The question on the impact of this better survival on the frequency of disability, has not been answered until very recently. Right now, the latest studies published show that outcomes have improved for children of weights between 1000 and 1500 grams and in those whose weight is lower than 1000 grams the frequency of disability is the same but has not increased²⁸.

The other positive aspect has to do with the movement in the Neonatal Units to change the way these children are treated. As has been exposed the Care centered on development has as a purpose to favour the neurologic and emotional development of the child. In every manipulation extreme care is taken to protect the fragile organism of the child and the necessary support is provided to maintain the patterns of conduct the most structured as possible. The impact of this care has still to be measured and large studies are still necessary but the provisional results are very positive²⁹. There is no doubt that prematurity is a primary health problem. Prevention and the best care of premature children and their families requires the attention not only of the health care system but also social, educative services and including from the working environment.

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