

Can we reduce worldwide neonatal mortality?

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Abstract. Worldwide neonatal mortality rate is still very high in many countries, with a sharp difference between developed and developing countries. The difference of interventions to be implemented for reducing neonatal mortality rate in developing and developed countries will be discussed. (www.actabiomedica.it)

Key words: neonatal mortality rate, Gross Domestic Product, equipment, education, health policy

Introduction

Pregnancy, delivery and birth are, by definition, physiological processes. Physiology derives from ancient Greek φύσις (= nature) and λογία (= study of), and means the study of functions in a living system (1).

Whereas physiological states refers to the normal functions of living organisms, pathological state refers to abnormalities caused by physical or mental diseases.

According to WHO data from 2015, more than 300,000 women each year die from complications tied to pregnancy and delivery, while another ten millions women each year suffer complications from lesions, infections and diseases due to pregnancy and birth that can last a lifetime (2). It has been calculated that the “maternal mortality lifetime risk” (an index related to pregnancy, birth, and fertility rate too) is 1:39 for an African woman and 1:4,700 for a European or North-American woman. This difference is due to many factors (2).

From 1990 to today the maternal mortality has been halved, but it is still very relevant in many countries, especially in those with lower income levels. To give an example, in India it is reported that approximately 80,000 women die every year for causes tied to pregnancy and/or delivery (2).

According to WHO data from 2019, 6,700 newborn infants die worldwide every day (3). This amounts to a minimum death rate of 4 newborns every minute.

About 75% of all neonatal deaths occurs in the first week of life, and 1 million of newborn infants die within the first 24 hours (3).

The same source reports that the worldwide neonatal mortality (mortality 0-28 days) has been drastically improved from 1990, reducing from 5 millions in 1990 to 2.4 millions in 2019, yet this represents a slower than for post-neonatal under-5 mortality (3,4).

No other so called “physiological” event can so frequently turn into a “pathological” one with often lethal condition as pregnancy and birth.

Furthermore no other physiological condition is wanted and awaited with as much joy and wonder by a couple as pregnancy and the birth of a new baby.

Many factors influence outcome of pregnancy, delivery, birth and the neonatal period. Very often these factors are the same. Identifying and improving them can contribute to a reduction of complications during both pregnancy, birth and the neonatal period.

In this paper only the conditions influencing the neonatal mortality and its possible corrective factors will be considered. As stated above, many of these factors and corrective actions are supposed to improve “maternal mortality lifetime risk” as well helping to increase the possibility that a physiological event remains as such.

Neonatal Mortality Rate Data

The reported decrease in neonatal mortality rate in the last 30 years differs according to which countries are taken into account, and even if the decrease globally amounts to 50%, there remains a great difference in the mortality rate X 1,000 live births observed between the areas where welfare is advanced and those of developing countries (Tab. 1).

If we look at the countries presenting the highest mortality rate in 2019, these are also those countries with the lowest income per person, e.g. neonatal mortality rate X 1,000 live births in Afghanistan is 36, in Somalia 37, in Central African Republic 40, in Nigeria 36, in Pakistan 41.

The lowest mortality rate is certainly dependent on higher income per person (Tab.2) but also on other factors: this is well shown by the fact that some countries at high Gross Domestic Product per person (GDP) as U.S.A. (63,544 US\$) are not present in the first 20 countries with the lowest neonatal mortality, and have a neonatal mortality rate of 4/ 1,000 live births, 25-75% higher than other developed countries (Tab.2) (5,6).

Table 1. Percent lowering of worldwide neonatal mortality rate X 1,000 live births: 1990 vs 2019 (mean values)

WORLD AREA	1990	2019	Δ %
Sub Saharian Africa	42.3	27.5	- 35.0
West and Central Africa	48.0	30.8	- 35.9
Eastern and Southern Africa	42.7	23.8	- 44.3
Middle East and North Africa	27.8	12.3	- 55.8
South Asia	58.7	25.1	- 57.2
East Asia and Pacific	27.5	7.2	- 73.8
Latin American and Caribbean	22.5	9.1	- 59.6
North America	5.6	3.7	- 34.0
Europe and Central Asia	14.0	4.4	- 68.6
Eastern Europe and Central Asia	20.5	6.0	- 70.7
Western Europe	5.6	2.3	- 58.9
World	36.6	17.5	- 52.2

(from WHO ⁽³⁾, modified)

Table 2. Neonatal mortality rate and Gross Domestic Product (GDP) (from (5,6) modified)

Country	Neonatal Mortality Rate / 1,000 Live Births (yr 2019)	GDP Per Person, US \$, (yr 2020)
Slovenia	1	25,180
Singapore	1	59,798
Iceland	1	59,261
Sweden	1	51,926
Japan	1	40,113*
Finland	1	49,041
Monaco	2	196,513*
Czech Republic	2	22,762
Spain	2	27,057
Australia	2	51,812
Italy	2	31,676
Republic of Korea	2	31,489
Israel	2	43,611
Luxembourg	2	115,874
France	3	38,625
The Netherlands	3	52,304
Germany	3	45,724
Canada	3	43,242
Switzerland	3	86,603
United Kingdom	3	40,285

* yr 2019

Data Analysis

Essentially the previous tables underline that countries can be subdivided in two great categories:

- a. High vs low neonatal mortality rate.
- b. High vs low GDP per person.

There is a strong interaction between the two categories. Indeed the data show that having a low GDP per person is related to high neonatal mortality. However having a high GDP per person does not always mean achieving the best neonatal

mortality. It is therefore clear that GDP by itself is necessary but not sufficient to guarantee the lowest mortality rates.

At the same time it is evident that if the goal is to reduce further neonatal mortality, the issues to be faced are different in the countries with high neonatal mortality and low income vs those with low/acceptable neonatal mortality and high income.

Countries with high neonatal mortality and low income

It may appear easy to reduce a very high percentage of mortality with minimal interventions. However when we take into account the obstetric and neonatal problems/interventions of these countries they are :

1. Mainly healthcare related:
 - Adequate structures for care: hospitals, on-site and itinerant outpatient clinics to favour control of pregnancy, delivery in the hospital and infant checkups.
 - Adequate transport system for mother and newborns.
 - The constant drugs' availability.
 - Adequate equipments to monitor pregnancy.
 - Adequate equipments to care for the newborn, both for normal fullterm babies, for those suffering from a disease, and the pre-term infants.
 - Education of health personnel and the development of adequate skills for the use of equipments.
2. Mainly socio-sanitary related:
 - Water supply.
 - Electricity supply.
 - Drainage systems.
 - Programs of development and control.
 - Campaigns to favor mass vaccination against preventable diseases.
3. Mainly socio-political related:
 - Battles against pollution, malnutrition, wars
 - Jobs and both their availability and the possibility of maternity leave.

- Intervention on the practice of some countries to sanction the abortion of female fetuses and the early neonatal death of female babies.

As many of these issues overlap it is not easy to consider most in isolation.

For the same reason, it is difficult to identify which issue is the most important to prioritize while it must be recognized that in many countries there is already some work in progress. Below we propose priorities for interventions even if it is clear that some of them have to be developed together:

- Certainly aqueducts supplying drinkable water largely reduce the risk of water transferrable diseases (e.g. schistosomiasis).

Water to irrigate plantations is one of the first need in many countries, as well as introduction of a drainage system.

Electricity supply: many of these countries have natural resources as oil or gas, but all too often their resources are exploited by the developed countries. Besides these countries must be empowered to use renewable energy sources.

- Hospitals and outpatient clinics, also itinerant offices and an effective transport system to reach people in difficult areas, are certainly the second point to be developed. It is clear that hospitals, clinics and transport systems have to be managed by educated personnel, both doctors, nurses and midwives and that the personnel is preferably chosen among the locals, which avoids the need of an interpreter.

Drugs, antibiotics especially, must be available. Too much of the neonatal mortality is due to infections and might be treated with adequate services and care. Drugs must be of course accompanied by sterile and disposable needles and syringes of the suitable size, infusion lines, infusion pumps, rehydrating solutions and oxygen (it has been calculated that every 39 seconds a child die from pneumonia potentially curable with antibiotics and oxygen (7)). Last but not least, support must be at

hand for lactating mothers. Simple procedures as ocular prophylaxis of ophthalmia neonatorum and of Chlamydial infection, Vitamin K prophylaxis at birth and adequate care of the cord are simple and cheap procedures that reduce mortality and morbidity.

These primary interventions need to be accompanied by:

- Improving the level of education at every level through development of continuous education programmes in the field of medicine, management of pregnancy, delivery and resuscitation of the neonate, and in the use of diagnostic equipment.
- Performing a vaginal swab to all pregnant women at 36 wks' gestation to evidenciate the presence of *Str. agalactiae* and carry out an intrapartum antibiotic prophylaxis if positive.
- Administering vaccines during pregnancy to prevent severe diseases (e.g. COVID 19 or pertussis or influenza) or giving specific treatment for infections acquired during pregnancy (e.g. Toxoplasmosis, Syphilis, Malaria, TBC and CMV)
- Promoting campaigns of pediatric mass vaccination. They have not a direct effect on the neonatal mortality - in fact the only preventable disease in the neonate at birth with vaccination is Hepatitis B - but they are certainly important for future pregnancies, because the control of the immunologic state of the pre-pregnant/pregnant women can evidenciate diseases treatable with drugs (e.g. syphilis, TBC, malaria), and check the serology of diseases preventable by prenatal vaccination (e.g. rubella) leading to the avoidance of abortions or severe fetal malformations.

These interventions have to be coordinated, to be constantly available and equally diffuse within the country. Therefore the health policy of each country have to establish which level of care can be provided and guaranteed as a minimum to the whole population. Besides methods of control on private and public

services with the scope of improving effectiveness and efficiency of the health system have to be supported.

Equipments in particular

Ultrasound machines with color-Doppler option, pulseoximeters, cardiocographs, multiparameters monitors, neonatal beds with radiant warmers and incubators, phototherapy lamps, transcutaneous bilirubinometers, bedside glycemia measurement devices, cartridge point-of-care laboratories, are essential as is education to their use.

Role of organizations

Non governmental no-profit local and international organizations can prompt campaigns for fund raising targeted to achieving the above mentioned objectives.

International political organizations should instead concentrate on helping to end disputes and wars through diplomacy, with the objective of reestablishing a normal lifestyle.

Countries with low/acceptable mortality rate and high income

How can one succeed in reducing neonatal mortality in countries, with the financial resources to do so and in which the main steps in protecting the care of mother and infant have been already developed? Why is it that some of these countries achieve at least 50% lower mortality rate than in other countries of the same high income standard? They have well educated personnel, with structures that, more often than not, represent the gold standard in state of the art, diagnostic equipments, outpatient clinics available from the beginning of pregnancy and a policy of aware parentality, neonatal services available in almost every point of birth and services of inter-hospital emergency transport of the mother before delivery or of the infant after birth. Newborn can be offered non-invasive ventilation in most of the perinatal centers, mechanical ventilation and inhaled nitric oxide in almost every Neonatal Intensive Care Unit (NICU), as well as therapeutic hypothermia in hub NICU centers and Extra-Corporeal

Membrane Oxygenation in a limited number of centers identified by experience and resources.

Some points need to be discussed:

- Which is the realistically obtainable lowest neonatal mortality rate?
- Only few of these countries have a neonatal mortality rate between 1-2/1,000 live births.
- It would seem impossible that in the first 20 countries with the lowest neonatal mortality there are not countries as U.S.A., where research is maximally supported.

Certainly there are a number of deaths that at present are not avoidable, as e.g. severe malformative syndromes, severe sepsis, severe asphyxia at birth, severe persistent pulmonary hypertension, Sudden Unexpected Post-natal Collapse, Sudden Infant Death Syndrome.

We must also take into account the different kind of babies that is born in the perinatal centers of these countries; in fact if in the low-income countries the target is to save first of all fullterm infants without severe malformations, in the high-income countries instead the target is to save babies with least chance of survival too. Therefore the neonatal mortality rate near to zero for fullterm infants is mixed with the very high mortality rate of babies in the range 22-26 wks' gestation, resulting in a figure that represents the mean. From the available raw data it is not possible to compare and explain the difference in the number of tiny babies in each of these countries because of the differences in how each collects and collates information.

In order to reduce mortality in these countries we must improve our knowledge of the mechanisms of premature delivery and act against them. Research is very useful, but also simple history, if well done, can help to identify and disclose problems.

Adequate structures, equipments and skills are equally necessary. Education for personnel has to be ongoing as does the upgrading of equipment to ensure it is always state of the art.

Close contact with the mother and the parenting couple is necessary, because their collaboration in care is essential.

It is also essential that such care is given to every family. In certain countries, however, these services are

upon payment, and insurance companies often do not cover all the expenses. In others they cannot be given to all. To limit deaths to the very minimum, inequality present both within and between countries must be tackled through socio-political engagement.

Where welfare is more developed, usually the number of children born per family is lower. However these babies must be healthy independently by their gestational age. Educating children in the best schools is expensive as is the cost of raising them and ensuring that they enter the workforce at a suitably high status and consequently level of pay. All these requirements create difficulties for a normal family to have more than 2-3 children. At present the challenge is to avoid survival of babies, especially tiny babies, with long-term disabilities, which will require life-long support. To reduce mortality while increasing disability is not the right way forward.

Therefore in this case solution can pass from a reform of NHS that is more inclusive of services for pregnancy and delivery and care of infants, the improvement of transport services both for the pregnant woman and for the neonate, and especially more uniform availability of these services country wide.

Unexpectedly in these countries skin to skin contact and breastfeeding must be better supported, something which occurs naturally in low income countries where these benefits are often the only possible and easy methods for mothers to guarantee warmth and food to their baby.

Discussion

As one might expect it seems much more difficult to achieve a further decrease in mortality in the developed countries. We would be happy if in these countries we can obtain a strong reduction in disability in the tiny babies that do survive. Preterm infants represent about 10-15% of all births but they consume immensely more money to be cared for. It is important that a premature birth can be foreseen: it can sometimes be accomplished with history and clinics, but more often it needs blood exams, ultrasound studies as well as cardiotocography. Prematurity is more severe at the lowest gestational ages where identifying the risk

of a preterm delivery at the realist possible moment will be crucial in guaranteeing the safety of the mother and fetus through a better organized perinatal unit with a dedicated transport service.

While the developed countries have invested many resources in the last 40 years to support the critical neonate, both at term and preterm, allowing survival of babies from 22 wks' gestation, with all the future needs of such survivors in terms of handicaps' support, it must be said that these efforts have also permitted survival of term and preterm infants without long-term consequences.

Where money is not available for the purchase of expensive equipments or the development of adequate facilities, other aspects have to be cultivated as they can save many term infants and reduce the number of preterm deliveries that in those countries presently die.

It is universally recognized that the first hour of life is the most important both for term and preterm infants alike but the first week of life is that in which the risk of dying remains high. The risk reduces during the first month of life, but the instability of the neonate remains and a matter of few hours can change the outcome of a disease of a neonate. Therefore it is necessary to ensure that a pediatric service is available on 24 hrs basis to recognize and treat the onset of a disease.

The current SARS-Cov-2 pandemia has shown that we cannot insulate within our borders and if we wish to resolve a problem we all have to collaborate altogether.

Before anything else underdeveloped countries must support the universal cares for the mother and the newborn infants.

The rich countries must give education, structures, equipment, without forgetting that i) drinkable water is a fundamental need of some countries, as well sewage system, ii) that equipment does not work without electricity and this should be achieved through a sustainable power source, iii) that equipment is only helpful if it comes with the training needed to use it and with the backup of local technical assistance and available spare parts.

Oxygen is a necessity and it can easily be obtained using oxygen concentrators. Adequate materials for neonatal use are disposable but for much equipment autoclavable materials are available. Surgical irons are autoclavable too.

In conclusion the needs required to improve the survival of neonates in developing countries are many: education, cheap and quickly raising of hospital structure, oxygen, drugs, ultrasound machines both for mother and infant, monitoring system (cardiotocography, vital parameters monitor), transfer unit, incubator and or neonatal intensive care beds, radiant warmers, phototherapy lamps, cartridge blood analysis including blood gases, pumps to infuse liquids are all required. Nothing of these can work without educated health personnel.

In developed countries great care must be taken to give the preterm infants the same care of the full-term health neonate and to reduce intra- and inter-countries' inequalities.

Our final goal in the perinatal field must be that of avoiding so many physiological processes turn into pathological states. This must be a global programme.

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