EVIDENCE-BASED INTERVENTIONS
REDUCE MATERNAL AND NEONATAL MORBIDITY AND MORTALITY
Manual

Belize 2015
EVIDENCE-BASED INTERVENTIONS REDUCE MATERNAL AND NEONATAL MORBIDITY AND MORTALITY

MANUAL

Francisco Martínez Guillen
Pediatrician- Neonatologist- Pulmonologist.
Former sub regional/temporary consultant PAHO/ WHO in Neonatal Health

Belize 2015
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Acknowledgements

This resource manual was developed in partnership with the European Union and the Pan American Health Organization. The objective of the resource manual is to provide health care workers with evidence based interventions known to contribute to the reduction of maternal and neonatal morbidity and mortality. For ease of reference in each of the topics, the interventions are placed within two orange color lines.

Dr. Francisco Martinez Guillen is the Consultant who conducted the research and wrote the manual. Consultations at all level of care and Ministry of Health Headquarters was conducted. The following local experts / organizations were invited to review the manual and provide feedback to the consultant: Robyn Daly, Sharon Anderson, Augustina Eljio, Jorge Polanco, Joycelyn Gonzalez, Marvin Manzanero, Ramon Figueroa, Samira Gongora, Arik Lima, Veronica Rosado, Renato Howe, Ruth Gough, Javier Zuniga, John Arana, Tracy Nicholas, Mirta Ochoa, Adrian Coye, Marcello Coyi, Jose Salinas, Joan Burke, Guillermo Rivas, Oneida Smith, Omar Garcia, Maria Montenegro, Carlos Ayala and Natalia L Beer; Lily Mahung, Leonie Castillo, Catherine Godinez, Lorita Haylock, Cynthia Guild, Isadora Espadas, Adelita Belle, Belize Pediatric Association, the Belize Medical and Dental Association. Presentations were done with health care workers from the different districts [Corozal, Orange Walk, Belize, Cayo, Stann Creek and Toledo] and Karl Heusner Memorial Hospital.
Introduction

The global commitment to achieve the Millennium Development Goal (MDGs) is to reduce by two thirds the mortality rate among children under 5 years of age and MDG 5 improve maternal health by reducing three fourth the maternal mortality ratio between 1990 and 2015 has led countries in the region to increase efforts and achieve significant reduction in both indicators. But neonatal mortality is the mortality rate that has decreased less, therefore is necessary to accelerate the reduction of neonatal mortality to achieve the MDG 4, more emphasis on prevention and treatment of morbidity and severe morbidity of maternal and neonates is required; this also implies reducing inequality between countries and within countries, between people of higher and lower income and between rural and urban populations.

There is a growing certainty that maternal-fetal and neonatal health are intimately linked and that simple cost-effective interventions, proposed in this manual and implemented in a continuum of care from pre-conception period, pregnancy, childbirth and postpartum and the network of care from the community to the referral hospitals can reduce both the morbidity, severe maternal morbidity and fetal and neonatal mortality and morbidity.

In a study of WHO published in 2013 in 29 countries in Asia, Africa and Latin America, pregnant women were compared to 2 groups, which had severe maternal outcomes (maternal death and near miss) morbidity and who did not have severe maternal outcomes. The main causes present in pregnant women with severe maternal outcomes (SMO) were: hypertensive disorders 30%, postpartum hemorrhage 27%, infection (sepsis, pyelonephritis, endometritis) 12%, abortion and ectopic pregnancy 15% and severe anemia was present in 34% of the other causes. In the children of pregnant women with SMO compared with those without SMO, there was increased mortalities: early neonatal, fetal and perinatal up to 7, 19 and 15 times respectively, increase in preterm infants by 4 times and NICU admissions by 5 times. (Table 1)

<table>
<thead>
<tr>
<th>EVENTS</th>
<th>Total Women Events x 1000LB</th>
<th>Women without SMO Events x 1000 LB</th>
<th>Women WITH Severe Maternal Outcome Events x 1000 LB</th>
<th>INCREASED RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Neonatal Mortality</td>
<td>8.8</td>
<td>8.6</td>
<td>63.5</td>
<td>7.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Fetal Mortality</td>
<td>21.0</td>
<td>19.4</td>
<td>370.0</td>
<td>19.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Perinatal Mortality (&gt;1 kg)</td>
<td>25.9</td>
<td>24.3</td>
<td>372.0</td>
<td>15.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Preterm Newborn [NB]</td>
<td>68.3</td>
<td>67.3</td>
<td>285.0</td>
<td>4.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Admission to NICU</td>
<td>67.1</td>
<td>66.0</td>
<td>310.3</td>
<td>5.0</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

* Severe Maternal Outcomes: maternal death or near missed cases
The Neonatal Mortality Rate in Belize has remained unchanged in the last five years (11.2 in 2009 to 11.4 / 1,000 LB in 2013). The main causes of death are those related to the perinatal period [prematurity, slow fetal growth, birth asphyxia, among others] secondary to maternal or fetal risk factors.

In 2011/2012 the Belize Nutrition Survey showed the following results:

- **Overall results**

National and regional geometric means of RBC folate among non-pregnant women of childbearing age, Belize 2011-2012, 729nmol/L, below the RBC folate sufficiency level 906 nmol/L.

- **Non-pregnant women [n 937]**

Anemia is a moderate public health problem (22.7%) (Range: 14.0%-30.5%). Severe and moderate anemia are low; Ferritin deficiency with and without the presence of inflammation was 17.8% and 26.0%. Ferritin deficiency is a moderate public health problem; Retinol deficiency was very low (1.2%) Great success; Serum and RBC folate deficiencies were low (4.1% and 6.8%, respectively); Folate insufficiency (68.6%) and combined vitamin B12 deficiency and marginal deficiency (50.4%) are a severe public health problem.

- **Pregnant women [n 71]**

Table 2. Ferritin deficiency with inflammation is a moderate public health problem

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>18.4</td>
</tr>
<tr>
<td>Ferritin deficiency (AGP&lt;1)</td>
<td>15.3</td>
</tr>
<tr>
<td>Ferritin deficiency (AGP≥1)</td>
<td>25.6</td>
</tr>
<tr>
<td>Retinol deficiency</td>
<td>0.0</td>
</tr>
<tr>
<td>Serum Folate deficiency</td>
<td>3.0</td>
</tr>
<tr>
<td>RBC folate deficiency</td>
<td>3.1</td>
</tr>
<tr>
<td>Folate insufficiency</td>
<td>57.9</td>
</tr>
<tr>
<td>B12 deficiency</td>
<td>46.4</td>
</tr>
<tr>
<td>B12 marginal deficiency</td>
<td>37.1</td>
</tr>
</tbody>
</table>

- **Children 6 to 59 months [n 971]**

Anemia is a moderate health problem (20.6%); Severe and moderate anemia were low (0.8% and 3.1%, respectively); Ferritin deficiency with and without the presence of inflammation was 13.2% and 30.5%; Ferritin deficiency with the presence of inflammation is a moderate public health problem (30.5%); Retinol deficiency was very low (1.0%); Serum and RBC folate deficiencies were low (0.9% and 6.0%, respectively); Vitamin B12 deficiency and marginal deficiency were 6.3% and 13.2%; Combined vitamin B12 deficiency and marginal deficiency are a moderate public health problem.
The National NTD's prevalence (per 1,000 LB) for Belize [Belize Surveillance System 2006-2009[Retrospective neural tube defects study] and 2012[National surveillance system of observable congenital malformations] is 1.1 and 1.7 respectively.

The purpose of the preparation of this manual on evidence based interventions (EBI) is to reduce maternal - neonatal morbidity and mortality, we've selected interventions that have been proven to be cost effective, based on the best evidence available globally and applicable to the country and can be used in the continuum of care from the first level of care to regional or national hospitals and from preconception period, during pregnancy and postnatal care, to prevent or treat the main causes associated with the country’s maternal and neonatal morbidity and mortality.

For the preparation of the manual, an intensive search was conducted in the best libraries in the world: Trip database, SUMSERCH, Hinari, Cochrane, Clinical Evidence, Clinical Queries, PubMed, MEDLINE searches Plus, Bireme, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Agency for Healthcare Research and Quality (AHRQ), National Guidelines Clearinghouse (NGC), among others.

Interventions that improve health or reduce morbidity and mortality both maternal and neonatal applying the GRADE system (Grading of recommendations, Assessment, Development, and Evaluation) to evaluate the quality of evidence were selected. The selected interventions were reviewed by a group of local experts with emphasis on applicability within the national context.

For best maternal and neonatal outcomes is essential to incorporate this evidence in the Ministry of Health guidelines, standards or protocols, the availability of necessary inputs (drugs and equipment), train health care workers [HCW], implement interventions and monitor compliance with the implementation.

Similarly it is required to perform an extensive process of training the trainers of human resources, clients, family and the general public.

It is also necessary to create the preconception care as an intervention for safe pregnancy. HCW should use existing attention spaces to educate the population in family planning, vaccination or consultation of children in waiting rooms, hospital. Also these interventions can be disseminated in schools, community centers and churches.

Criteria for Evaluating the Quality of Evidence

Table 3 GRADE, Criteria quality of the Evidence

<table>
<thead>
<tr>
<th>Quality of the evidence</th>
<th>Study design</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Random Control Trials [RCT]</td>
<td>Improbable that effects will change with new studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>Low quality RCT</td>
<td>Probable change of effects with new studies</td>
</tr>
<tr>
<td>Low</td>
<td>High quality observational studies</td>
<td>Very probable that new studies will change the effects</td>
</tr>
<tr>
<td>Very Low</td>
<td>Any other evidence</td>
<td>Uncertain estimated effect</td>
</tr>
</tbody>
</table>
The guidelines OR manuals are as good depending on how good the evidence and the critical analysis on which they are based. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) is a system for assessing the quality of the evidence and strength of the recommendations (Table3). The GRADE approach aims to facilitate users to evaluate the critical thinking behind each recommendation.

The biggest advantage of the GRADE system compared to other classification is that it provides a practical recommendation for each intervention, assessing trust and adherence to the more beneficial than harmful recommendation. The recommendation is based on the quality of the evidence, how evidence can be applied in specific settings (e.g. low-and middle-income countries) and the ratio of benefits, risks and costs.

The recommendation for each procedure is placed in one of the following categories:
- Strong in favor
- Weak in favor
- Weak against
- Strong against

The recommendation against the intervention does not necessarily indicate that there is evidence that it is harmful; it often reflects no evidence of benefits and costs, no reason for its application.

Some concepts to assess Evidence.161-164

OR: odds ratio (odds ratio, odds ratio, or ratio of odds). It is the odds ratio of having the designated experimental group relative to the odds of having the designated control group (cohort studies or systematic reviews) disorder or the odds in favor of being exposed in subjects with the disorder divided by the odds in favor of being exposed in control subjects (without the designated disorder). It measures the strength of association applied to all types of studies using nominal data, but usually applies to case-control studies and cross-sectional studies.

RR: relative risk. Ratio of the probability that an outcome occurs in a given period, exposed to the risk factor and the probability of occurrence among the unexposed to the risk factor in the same period. The RR is a measure of the strength or degree applicable to cohort studies and RCT partnership. In the case-control OR can be used as an approximation to the RR.

SR: Systematic Review. It’s a summary of the medical literature that uses explicit methods to search cites systematically, critically evaluates and synthesizes the world literature on a specific problem. Its goal is to minimize both bias and error randomization.

CI: Confidence interval. It is a measure of the uncertainty around the main finding of a statistical analysis. The estimates of unknown quantities, such as the OR comparing an experimental intervention with a control, usually presented as a point estimate and a confidence interval of 95%, this means that if you repeat a study in other samples of the same population, 95% confidence intervals [CI] of these studies contain the true value of the unknown. A wide CI indicates very low precision, short CI indicates exact precision.
Interpretation of RR, OR and IC

If the:

• RR or OR = 1, or CI includes 1 (RR 1.00 i.e., 95% CI 0.49 to 2.48), is interpreted as non-significant statistical difference between the group receiving the treatment and the control group.

• RR > 1 and the CI do not include 1 (events are statistically significant more likely in the treatment group than in the control).

• RR < 1 and CI does not include 1 (RR 0.67 e.g. 95% CI 0.45 to 0.99), the events are statistically significant less likely in the treatment group than in the control group.

Bibliography


Interventions in preconception period

1. Birth Spacing (pregnancy interval - achieve optimal range).

Background

In Latin America and the Caribbean (LAC) sub-region the average range between pregnancies is 28 months, 18% is <12 months and 19% ≥ 60 months. Pregnancy interval <12 months is more common in young women, with late onset and fewer antenatal monitoring, history of LBW, abortions and perinatal death. Women with pregnancy intervals ≥ 60 months were more often: older, with adequate antenatal care, increased pre-pregnancy and pregnancy BMI, live born and healthy.

Definition

Pregnancy interval is the time between the birth of a child and the next pregnancy.171

Interventions

A. Pregnancy Spacing (Strong recommendation, high quality evidence)

A.1 After a live birth. Pregnancy interval ranges from 2 years to less than 5 years, with proper counseling and reproductive health education and family planning services. (Strong recommendation, high quality evidence to reduce maternal, fetal, neonatal, infant and under 5 years mortality, preterm births, low birth weight infants small for gestational age [SGA] and Autistic Disorder) 1,2,186,187,194,195.

A.2 After an Abortion. It is recommended that the minimum pregnancy interval be 6 months to reduce the risk of adverse maternal and perinatal outcomes.171
Evidence\textsuperscript{1,2}

It has been estimated that the promotion and achievement of adequate spacing in countries with high birth rates can reduce 33\% of maternal deaths and 10\% infant mortality\textsuperscript{1}.

In LAC (Table 4) the Latin American Center for Perinatology (CLAP)\textsuperscript{2} in [n=1125430] women found that pregnancy interval <6 months compared to 18 to 23 months had increased risk of early neonatal mortality by 49\%, fetal death 54\%, LBW 88\%, preterm births 80\%, very preterm 95\% and SGA infants 30\%. Pregnancy intervals of 6-11 months and > 60 months were also significantly associated with the same adverse perinatal outcomes.

In another meta-analysis (MA)\textsuperscript{1} increments of 40\% of preterm births was found when the interval was <6 months compared to 18-23 months intervals (RR 1.40, 95\% CI 1.24-1.58) and 20\% (OR 1.20, 95\% CI 1.17-1.24) increase in preterm births when the interval was ≥ 60 months.

In a recent study, Bloomberg School of Public Health, Johns Hopkins University,\textsuperscript{186} US, with data from 47 demographic and health research of middle-and low-income Africa, Asia, Europe and America, assessed the relationship of birth intervals and neonatal and under 5 years mortality rates (U5MR). Taking as ideal reference the births intervals in mothers between 24 - <60 months. Mothers with high parity when intervals were < 24 months, neonatal mortality was increased 61\% (OR 1.61, 95\% CI 1.52-1.70) and U5MR 48\% (OR 1.48, 95\% CI 1.40-1.56). When the interval was < 18 months, there was 82\% increase in neonatal mortality (OR 1.82 95\% CI 1.55-1.79) and U5MR 66\% increase (OR 1.66 95\% CI 1.55, 1.79). When the birth interval was ≥ 60 months [only in Asia but not in LAC] the neonatal mortality was reduced; the U5MR decreased in Africa, Asia and the Americas by 30-40 %.

In a meta-analysis from Johns Hopkins\textsuperscript{187} University from 5 multicenter cohort (including Brazil) n=32,670 of live births, the birth interval <18 months significantly increased child mortality by 83\% (OR 1.83, 95\% CI 1.19 - 2.81), preterm births by 58\% (OR 1.58, 95\% CI 1.19-2.10) and newborns small for gestational age 51\% (OR1.51, 95\% CI 1.31-1.75)\textsuperscript{4}.

A study in California\textsuperscript{194} with n662, 730 an inverse relationship between pregnancy interval and risk of autism in the second child was found. Intervals <12months, 12 to 23 and 24 to 35 months compared with ≥ 36 months were respectively with the OR (95\% CI), 3times 3.39(3.00-3.82), 2 times 1.86 (1.65-2.10), and 26 \% 1.26 (1.10 -1.45) increase the risk for autism.

In Norway\textsuperscript{195} n=223 476 in single brothers with pregnancy interval <9 months the adjusted risk for autistic disorder was twice(OR 2.18, 95\% CI 1.42-3.26) and the range of 9 - 11 months increased the risk by 71\% (OR 1.71, 95\% IC1.07 - 2.64).

The pregnancy interval <6 months after an abortion in LAC n=258 108 have high risk of: premature rupture of membranes, vaginal bleeding, anemia, preterm and very preterm births and LBW.\textsuperscript{171}
Table 4. Association between pregnancy interval and perinatal mortality in Latin America and the Caribbean sub region*

<table>
<thead>
<tr>
<th>Results</th>
<th>Adjusted Pregnancy Interval (months), OR (IC 95 %)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 6 m</td>
<td>12-17 m</td>
<td>18-23* m</td>
<td>&gt; 60 m</td>
<td></td>
</tr>
<tr>
<td>Early Neonatal Deaths</td>
<td>1.49 (1.06-1.96)</td>
<td>1.08 (0.96-1.21)</td>
<td>1.00</td>
<td>1.18 (1.07-1.31)</td>
<td></td>
</tr>
<tr>
<td>Fetal Demise</td>
<td>1.54 (1.28-1.83)</td>
<td>1.07 (1.00-1.15)</td>
<td>1.00</td>
<td>1.21 (1.15-1.27)</td>
<td></td>
</tr>
<tr>
<td>Birth Weight &lt; 2.5 kg</td>
<td>1.88 (1.78-1.90)</td>
<td>1.05 (1.00-1.10)</td>
<td>1.00</td>
<td>1.19 (1.15-1.24)</td>
<td></td>
</tr>
<tr>
<td>Preterm Newborn</td>
<td>1.80 (1.71-1.89)</td>
<td>1.05 (1.00-1.09)</td>
<td>1.00</td>
<td>1.20 (1.15-1.24)</td>
<td></td>
</tr>
<tr>
<td>Very preterm Newborn</td>
<td>1.95 (1.67-2.26)</td>
<td>1.04 (0.96-1.13)</td>
<td>1.00</td>
<td>1.16 (1.09-1.24)</td>
<td></td>
</tr>
<tr>
<td>Small for Gestational Age</td>
<td>1.30 (1.25-1.36)</td>
<td>1.03 (1.00-1.06)</td>
<td>1.00</td>
<td>1.23 (1.18-1.32)</td>
<td></td>
</tr>
</tbody>
</table>

* Reference Pregnancy Interval

After a live born the pregnancy interval should be at least 2 – 5 years, to reduce the risk of adverse maternal and neonatal outcomes.1,2

Bibliography

Birth Spacing


2. Preconception Nutrition Assessment with Body Mass Index (BMI) and waist circumference and its correction.

Background

Obesity in preconception period is associated with increased risk of stroke and cerebrovascular accidents. Overweight and obesity are significantly associated with: asthma, hypertension, cardiovascular disease, diabetes, dementia, depression, (breast, ovarian, endometrial cancer, leukemia, etc.), subfertility, abortions, birth defects, fatty liver, cirrhosis, cancer, obstructive sleep apnea, osteoarthritis and higher mortality.

The Body Mass Index (BMI) is a tool easy to apply for the classification of overweight and obesity in adults, an internationally accepted evaluation of nutritional status, applicable to both sexes and independent to age. BMI should be used to classify overweight and obesity in adults. The waist circumference (WC) is such a good indicator of total body fat and BMI and is the best anthropometric predictor of visceral fat.

WHO recommends that for assessing the risk of type 2 diabetes, hypertension and cardiovascular disease may be better to use both BMI and waist circumference (Table 5).

BMI is useful to assess nutritional status during the preconception period and to modify any abnormality to reduce its consequences before pregnancy (Table 5).

The Body Mass Index (BMI) is calculated by dividing weight in kilograms (kg) by height (height in square meters (m²)). BMI = weight in kg / height m²

BMI (kg / m²) Classification

- Obese: BMI > 30
- Overweight: BMI 25.0 - 29.9
- Normal: BMI 18.5 - 24.9
- Underweight: BMI < 18.5

Obesity
- Class I or mild obesity: BMI 30.0 - 34.9
- Class II or moderate obesity: BMI 35.0 - 39.9
- Class III or extreme obesity: BMI ≥ 40.0

The technique for measuring waist circumference (WC), recommended by the WHO and the International Diabetes Federation, patient is standing with their feet together, with tape on the horizontal plane to the floor, in the middle line between the edge of the lowest rib and the iliac crest, the tape measure snug against the skin but not tight and ends of a normal expiration (removal of the lung air). This way of measuring waist circumference is the best method especially in women.
Table 5. Classification of disease risk based on Body Mass Index (BMI) and waist circumference (WC). WHO

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (Kg/m²)**</th>
<th>OBESITY</th>
<th>Male WC 94 - 102 cm</th>
<th>Female WC 80 - 88 cm</th>
<th>Male WC &gt; 102 cm</th>
<th>Female WC &gt; 88 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Weight</td>
<td>18.5 - 24.9</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0 - 29.9</td>
<td>Increased</td>
<td>HIGH</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>OBESITY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>30.0 - 34.9</td>
<td>I</td>
<td>HIGH</td>
<td>VERY HIGH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>35.0 - 39.9</td>
<td>II</td>
<td>VERY HIGH</td>
<td>VERY HIGH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extreme</td>
<td>≥ 40.0</td>
<td>III</td>
<td>EXTREMELY HIGH</td>
<td>EXTREMELY HIGH</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Risk for Diabetes type 2, Hypertension and cardiovascular disease. **Increased WC is a predictor of increased disease risk even in persons with NORMAL WEIGHT***BMI: Body Mass Index = weight in Kg / height in m²

The average WC in men ≥ 94 cm and in women ≥ 80 cm indicate high risk of obesity-related diseases such as: type 2 diabetes, hypertension and cardiovascular disease.

Nutrition Definition

The process by which food substances are transformed into body tissues and provide energy for the full range of physical and mental activities that makes up human life.

Interventions

The purpose is to prevent overweight and obesity in those with normal weight and achieve weight reduction and maintain reduction in those who are overweight or obese:

a. Improve preexisting comorbidities related to obesity.

b. Reduce the future risk of obesity-related co morbidities

c. Improving the physical, mental and social well-being.

Prevention of overweight and obesity: (Strong recommendation, high quality evidence)

a. Counseling and education to avoid eating high-calorie foods: animal fat and sugars, fast food (takeaway), and alcohol.

b. Encourage the use of low-calorie foods: rich in fiber (cereals, rice, pastas, wheat flour) tortillas, fruits, vegetables, 3-5 servings a day (carrot, tomato, broccoli, celery, spinach, whole grain carbohydrates, cucumber, onions) and salads, 4
servings a day of low-fat milk, yogurt or dairy products (1 serving is 1 cup) intake of water instead of sugary drinks.

c. Encourage moderate physical activity (walking) 30-45 minutes per day at least 5 days a week.

Treatment for overweight and obesity (Strong recommendation, high quality evidence)

a. For women with BMI 25-35 kg/m², the obesity-related co morbidities are less likely to be present; a reduction of 5-10% by weight (approximately 5 - 10 kg) is required to reduce the risk of metabolic and cardiovascular disease.

b. If the BMI is > 35 kg/m², co morbidities related to obesity are likely to be present, so a sustained weight loss requires > 15-20% (always> 10 kg) to achieve a sustained improvement in co morbidities related to obesity.

The weight loss program should include: physical activity, dietary changes and behavior.

a. The Physical activity should be a caloric expenditure of 1800-2500 kcal / week corresponding to 225-300 minutes per week, 5 sessions of 60 minutes per week of moderate-intensity physical activity, such as brisk walking (respiratory rate is increased but you can talk comfortably). Sedentary people should start with physical activity 10-20 minutes / day in between, with progressive increase.

b. The diet for weight loss should be calculated to produce 600 kcal / day of calories deficit (energy) (lower consumption of carbohydrates and fats).

c. Individual or group psychological interventions (for behavior change), should be included in the weight reduction programs: includes self-monitoring of behavior and progress, stimulus control (where the patient is taught to recognize and avoid triggers an unplanned situations), power, cognitive restructuring (modification of negative thoughts and thought patterns), goal setting, problem solving, slow eating, reinforcement of changes and relapse prevention.

Evidence

Education for people to become aware of and actions to achieve the prevention or the sustained weight loss in overweight / obesity, decreases: morbidity and mortality from all causes of cancer, type 2 diabetes, hypertension, asthma, osteoarthritis, maternal and perinatal morbidity / mortality.4,5
3. **Periconception folic acid for prevention of neural tube defects**

**Background**

Neural tube defects (NTD’s) affects globally and by region an average range from 0.2 to 10 pregnancies / 1000, with higher frequency in spontaneous abortions. The relative frequency of NTD’s are: 50% myeloid- meningocele, anencephaly 40%, encephalocele 7%, craneorachischisis 3% unspecified dysraphism. Open injuries affecting the brain (anencephaly, craniorachischisis) they are lethal before or at birth. Encephalocele may be lethal depending on the extent of the brain damage. **Worldwide, more than 10% of high infant mortality rates are caused by Congenital Malformations (CM) - NTD’s.** In poor countries it is estimated that 29% of neonatal deaths related to observable congenital malformations (OCM) are attributed to NTD’s.

Folic acid deficiency (FAD) has been well identified as a teratogen factor that increases the risk of NTD’s. Folic acid [FA] favors the production of purines and pyrimidine for DNA replication during cell proliferation and the donation of methyl groups of macromolecules, including DNA, proteins, and lipids (epigenetic regulation of genes). Cell multiplication has a key role in closing the neural tube. The cause of NTD’s is multifactorial mono or polygenic with an important role of genetic factors.

The high risk factors for NTD’s are: personal or family history of NTD’s 30 times greater risk (RR 30), chromosomal abnormalities (trisomy 13, 18, 21), consanguinity, maternal pre-pregnancy and pregnancy diabetes (RR 2-10), obesity BMI > 30, anticonvulsant drugs.
(phenytoin, carbamazepine and valproic acid) 10 - 20 times (RR 10-20), maternal folate deficiency (RR 2-8). Other risk factors include maternal hyperthermia, tobacco, alcohol, poor intestinal absorption, renal and hepatic failure. Maternal Vit B 12 deficiency is a factor that doubles the risk of NTD’s OR 2.41 (95 % CI 1.90-3.06).

Peri-conception hyperglycemia in women with type 1 and type 2 diabetes diagnosed before pregnancy, there was a three to six fold increased risk across all common congenital anomaly and increase of major congenital anomaly was 4times RR 3.8 (95% CI 3.2, 4.5) compared with women without diabetes.

The neural tube closure occurs on day 28 post-conception, which is day 42 gestational age [GA]. Maternal folate concentration of 906 nmol / L in red blood cells is required to reduce the risk of NTD’s in offspring. This concentration is reached on average within 4 weeks at doses of 0.8 mg daily FA, and 8-12 weeks for dose of 0.4 mg FA per day, so it is recommended to increase folic acid intake up to 0.8 - 1 mg of FA / day.

Definition

NTD’s are birth defects of the brain and spinal cord. The most frequent NTD’s are: anencephaly, meningocele and myelo- meningocele, encephalocele and spina bifida. In anencephaly, much of the brain does not develop. In meningocele or spina bifida, the fetal spinal column does not close completely during the first month of pregnancy. Folic acid (FA) is the synthetic form of folate or vitamin B 9, and is more bioavailable than natural folate in food.

Periconception refers from 3 months before conception to 3 months after conception.

Interventions (Strong recommendation, high quality evidence)

   a. Prevention of Neural Tube Defects (NTDs) with Periconception folic acid (FA)

It is recommended that all women who are at risk or plan to become pregnant take FA for 3 months before pregnancy, throughout pregnancy and throughout lactation:

Women without risk factors for NTD’s: take multivitamins (MV) * with FA 0.8 to 1 mg / day orally (PO) for 3 months pre-conception up to 3 months post-conception. From 3 months post-conception throughout pregnancy and throughout lactation take a MV with FA 0.4 to 1 mg / day PO.

Women with a high risk factor for NTD’s: MV * and FA 5 mg / day PO for 3 months preconception up to 3 months post-conception. From 3 months post-conception throughout pregnancy and throughout breastfeeding MV with FA 0.4 to 1 mg / day PO.

Daily consumption of a diet rich in FA: green leafy vegetables (spinach, broccoli and lettuce), asparagus, avocado, fruits (oranges, lemons, bananas, melons), beans, black beans, meat (chicken, pork, fish, beef liver and kidney, tuna), the tomato juice, fortified oatmeal and wheat bran.
*The MV contains: 800 micrograms (0.8 mg) FA 6000 IU (until 1989) and 4000 IU (1990-1991) Vit A; 1.6 mg Vit B1; 1.8 mg Vit B2; 19 mg nicotinamide; Vit B6 2.6 mg; Ca pantothenate 10 mg; 0.2 mg biotin; 4.0 pg Vit B12; 100 mg Vit C; 500 IU Vit D; 15 mg Vit E (alpha-tocopherol acetate); 125 mg Ca; 125 mg phosphorus; 100 mg Mg, 60 mg elemental Fe; 1 mg Cu; 1 mg manganese; and 7.5 mg zinc

Evidence \(^9,^{12-15}\)

In RCT the MV with FA showed greater efficiency in NTD’s reduction \([> 90 \%]\) compared to FA alone \((71 \%)\) at high doses and 41 \% at low doses. In conclusion the MV with FA containing 0.8 to 1 mg is more effective in the prevention of NTD’s, than FA alone. \(^8,9\) FA alone also not reduces the other non NTD’s CM. \(^17\) The FA (alone or with MV) when used in Periconception (Table 6) reduces the risk of NTD’s: 72\% in the overall occurrence, first case by 93 \% and recurrence in 69 \%, neonatal mortality by NTD’s 13\% and 41 \% fetal mortality \((RR 0.59, 95\% CI 0.52 to 0.68)\). \(^{16,17,196}\)

Table 7 Periconception FA alone or combined with MV reduces the risk for NTD’s and fetal and neonatal mortality \(^{16,17,196}\)

<table>
<thead>
<tr>
<th>FA Reduces NTD’s</th>
<th>RRR %</th>
<th>RR</th>
<th>IC 95 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Global</td>
<td>72</td>
<td>0.28</td>
<td>0.13, 0.58</td>
</tr>
<tr>
<td>* Occurrence</td>
<td>93</td>
<td>0.07</td>
<td>0.00, 1.32</td>
</tr>
<tr>
<td>* Recurrence</td>
<td>69</td>
<td>0.31</td>
<td>0.14, 0.66</td>
</tr>
<tr>
<td>* Fetal Mortality due to NTD’s (^{196})</td>
<td>41</td>
<td>0.59</td>
<td>0.52-0.68</td>
</tr>
<tr>
<td>* NEONATAL Mortality due to NTD’s</td>
<td>13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Periconception use of MV containing 0.8 - 1 mg of FA is more EFFECTIVE in the PREVENTION OF NTD’s and reduces FETAL AND NEONATAL MORTALITY.

Bibliography

Neural Tube defects


4. Periconception multivitamins for the PREVENTION of non NTD’s Congenital Malformations [CM]

Background

The prevalence of CM is about 14% of total human fetuses; they are classified as major, severe or lethal CM [3%], and 11% lower or benign. Of the major CM, heart is 25%, 20 % limb and nervous system 10 %. The CM has increased by more than 25 % as a cause of infant mortality in developed and developing countries.\(^8\)

Definition

Congenital malformations (CM): Alterations in the structure and function of one or more body parts during in utero development.

Risk factors for the non-NTD’s congenital malformations

The proportion of birth defects according to the involved organs are\(^{210}\): central nervous system 20 %, face or eye 18 %, extremities 13%, cardiovascular 12%, skeletal 8%, Genitourinary tract 6 %, thoracic or abdominal wall 6%.

- The factors that may increase the risk of birth defects are: maternal age< 25 y, alcohol drinking, familiar inheritance, and lower education level of mothers, living in rural areas.\(^{210}\) Consanguinity was associated with a doubling of risk for congenital anomaly (RR 2·19, 95% CI 1·67-2·85); 31% of all anomalies in children of Pakistani origin could be attributed to consanguinity. Similar increase 83 % in risk for mothers of white British origin older than 34 years (RR 1·83, 95% CI 1·14-3·00).\(^{213}\)

- Peri-conception hyperglycemia in women with type 1 and type 2 diabetes diagnosed before pregnancy, there was a three to six fold increased risk across all common congenital anomaly and increase of major congenital anomaly was 4times RR3.8 (95% CI 3.2, 4.5) compared with women without diabetes.\(^{211}\)

-Among no diabetic women high maternal dietary glycemic index\(^{212}\) (higher carbohydrate ingestion), was significantly associated 3 times with encephalocele (adjusted OR (aOR) = 2.68), diaphragmatic hernia (aOR = 2.58), small intestinal atresia/stenosis (aOR = 2.97) including duodenal atresia/stenosis (aOR = 2.48), and atrial septal defect (aOR = 1.37), cleft lip with cleft palate (aOR = 1.23) and anorectal atresia/stenosis (aOR = 1.40). The joint effect of high DGI and obesity provided evidence of a synergistic effect on the risk of selected birth defects.
The Spina bifida (SB), 80% are classified as isolated, 20% as non-isolated. The non-isolated cases were accompanying of the major congenital defects: midline defects (brain reduction defects, imperforate anus, cloacal extrophy, diaphragmatic hernia, tracheoesophageal fistula ± esophageal atresia), renal, heart defects and genital defects. Only the isolated SB decreased in mothers achieving a folic acid intake ≥400 μg/day.

In studies in Florida, USA with n 1,334,431 and others CM prevalence increased significantly (p < 0.001) in obese women directly related to the increase in pre pregnancy BMI. The dose response relationship was at greater obesity for the following CM: cleft palate, diaphragmatic hernia, hydrocephalus without spina bifida, hypoplastic left heart, atresia and stenosis of pulmonary valve syndrome, atresia intestinal and rectal stenosis, pyloric stenosis, transposition of great arteries, ventricular septal defect and tetralogy of Fallot. Maternal fever during pregnancy or influenza may be associated with obstructive cardiac lesions, in all children with atrioventricular septal defects in children with Down syndrome, antipyretics attenuate such association. CM of the heart and limb was significantly associated with smoking or second hand smoking during the Periconception period.

A cohort study of all mother-infant pairs (n=2,278,838) in Canada, 2002 to 2010, the association between maternal conditions and congenital heart defects (CHDs) in infant using logistic regression with adjustment for maternal age, parity residence, and other factors. There were 26,488 infants diagnosed with CHDs; the overall CHD prevalence was 116 per 10,000 LB, of which the severe CHD rate was 22 per 10,000. Risk factors for CHD included maternal age ≥40 years (adjusted odds ratio [aOR], 1.48; 95% CI 1.39–1.58), multifetal pregnancy 4 times (aOR, 4.53; 95% CI, 4.28–4.80), diabetes mellitus 4 times (type 1: aOR, 4.65; 95% CI, 4.13–5.24; type 2: aOR, 4.12; 95% CI, 3.69–4.60), hypertension 81% (aOR, 1.81; 95% CI, 1.61–2.03), thyroid disorders 45% (aOR, 1.45; 95% CI, 1.26–1.67), congenital heart disease 10 times (aOR, 9.92; 95% CI, 8.36–11.8), systemic connective tissue disorders 3 times (aOR 3.01; 95% CI, 2.23–4.06), and epilepsy and mood disorders 41% (aOR, 1.41; 95% CI, 1.16–1.72), obesity 48% (aOR 1.48, 95% CI, 1.32–1.65), alcohol or substance use 88% (aOR 1.88 95% CI 1.74–2.04).

The lack of MV containing FA during the Periconception period can be associated with excess risk for CM due to diabetes.

The recurrence of certain CM as cardiac, limb, cleft lip, hydrocephalus and urinary tract may be decreased by Periconception MV and FA

Interventions (Strong recommendation, high quality evidence)

It is recommended that all women who are at risk or plan to become pregnant, take MV with FA for 3 months pre-conception, throughout pregnancy and while breastfeeding:

Women without risk factors for NTD’s and other CM: MV* with FA 0.8 - 1 mg / day orally (PO) for 3 months pre-conception up to 3 months post-conception. From 3 months post-conception throughout pregnancy and throughout lactation give a daily MV with FA 0.4 to 1 mg / PO.
Women with a high risk factor for NTD’s or other CM: MV * with FA 5 mg / day for 3 months preconception PO up to 3 months post-conception. From 3 months post-conception throughout pregnancy, and while breastfeeding, give a MV with FA 0.4 to 1 mg / day PO.

Daily consumption of a diet rich in FA: green leafy vegetables [spinach, broccoli and lettuce], asparagus, avocado, fruits (bananas, melons, lemons) beans, black beans, meat (chicken, pork, fish, beef liver and kidney, tuna), orange juice and tomatoes, fortified oatmeal and wheat bran.

*The MV contains: 800 micrograms (0.8mg) FA 6000 IU (until 1989) and 4000 IU (1990-1991) Vit A; 1.6 mg Vit B1; 1.8 mg Vit B2; 19 mg nicotinamide; Vit B6 2.6 mg; Ca pantothenate 10 mg; 0.2 mg biotin; 4.0 pg Vit B12; 100 mg Vit C; 500 IU Vit D; 15 mg Vit E (alpha-tocopherol acetate); 125 mg Ca; 125 mg phosphorus; 100 mg Mg, 60 mg elemental Fe; 1 mg Cu; 1 mg manganese; and 7.5 mg zinc.

Evidence

The use of MV in Periconception period reduces the major CM especially Heart, almost half (RR 0.53, 0.35 to 0.70), and further cardiac septal ventricular by 74% (RR 0.26, 0.09-0.72) 15,23,25

Bibliography

Periconception multivitamins for the Prevention of non-NTD’s Congenital Malformations


5. Prevention and treatment of iron deficiency anemia during preconception period

Background

Worldwide, the estimated number of women in reproductive age with anemia is 469 million. The overall average of anemia prevalence rate in women in the preconception period is 30.2%, with variations depending on the country from 7.6% in North America, 15.2% in Europe, 23.5% in Latin America and Caribbean (LAC) to 44.4% in Africa. In Nicaragua, preconception anemia prevalence rate decreased from 67% to 33.6% in 1993 to 11.2% in 2003/2005 with iron deficiency (serum ferritin < 15 ug/dL) of 31% in the latter period.

Iron deficiency (ID), is the cause of > 50% of the total cases of anemia secondary to low intake or poor absorption of iron, high iron requirements (pregnancy), blood loss (the most frequent in women in reproductive age [WRA] is menstruation and, intestinal parasites), malaria, infections (tuberculosis, HIV), cancer, deficiency of other micronutrients such as vitamins A, B12, folic acid, riboflavin and copper. Hemoglobinopathies also is considered in certain populations.

Iron deficiency anemia is the most severe and late stage of the iron deficiency. In several studies, moderate to severe anemia in the preconception period was significantly associated with preterm births 53% (OR, 1.53, 95% CI 1.05-2.23), low birth weight 6.5 times (OR 6.5, 95% CI: 1.6 26.7, p < 0.009 and slow fetal growth/ restriction 4.6 times (OR 4.6, 95% CI: 1.5, 13.5, p < 0.006)

Women who begin pregnancy with suboptimal iron stores are at high risk for adverse maternal and neonatal outcomes.
**Definition**

**Anemia:** It is the decrease in the amount of hemoglobin (Hb) or the number of red blood cells (RBC) in blood. Iron deficiency anemia (IDA) is anemia due to insufficient iron to maintain normal physiological functions of tissues such as red blood cell, brain and muscles. 

According to WHO, anemia in women ≥ 15 years, in the preconception period is defined with Hb < 12 g / dL (<120 g / L) at sea level.

Iron deficiency anemia (IDA) is diagnosed by the presence of anemia plus iron deficiency (ID) measured by the decrease in serum ferritin (< 15 ug / L) or an indicator of iron status e.g. serum transferrin receptor.

**The severity of Anemia according to the WHO** in the preconception period (non pregnant women ≥ 15 years), at sea level, anemia is in g / L or (g /dL) Hb: Mild anemia110 - <120 g / L (11 < 12 g / dL), moderate 80 - <110 g / L (8 < 11 g / dL) and Severe <80 g / L (<8 g / dL). No anemia ≥ 120 g / L (≥ 12 g / dL). (Table 7)

| Severity of anemia in pre-conception period in females ≥ 15 years, WHO |
|---|---|---|
| Anemia at sea level | Hb g / dL | Hb g / L |
| - No Anemia | ≥ 12 | ≥ 120 |
| - Mild | 11 a < 12 | 110 a < 120 |
| - Moderate | 8 a < 11 | 80 a < 110 |
| - Severe | < 8 | < 80 |

**Interventions (Strong recommendation, high quality evidence)**

**Prevention of Iron Deficiency Anemia in the Pre pregnancy period:**

**Strong WHO recommendation:** Intermittent supplementation of iron and FA, as a public health intervention for menstruating women in areas with high prevalence of anemia (≥ 20 % of non-pregnant), improves hemoglobin concentration, iron status and reduces the risk of anemia.

**Provide supplements to all menstruating women:** Adolescents and adults. Adolescents can be reached in schools. Plan the distribution in accordance with school calendar.

**Dose:** 60 mg of elemental iron plus FA 2.8 mg (2800 mcg) once a week for 3 months followed by 3 months without supplementation and restart. (The dose of 2.8 mg of FA can be achieved with: 1 tablet of iron and FA [0.4 mg] plus 1/2 tablet of 5 mg FA.

- Treat menstruating women with anemia according to the degree of anemia.
- In regions with high prevalence (> 20-30%) of intestinal parasites administer Albendazole 400 mg every 6 meses.31

**Treatment of Iron Deficiency Anemia during pre-pregnancy**32,33,35

Depending on the severity of the anemia, the recommended dose of elemental iron is 60-200 mg plus 0.4 mg folic acid / day / for 3 months (Strong recommendation, high quality evidence)

**Elemental Iron Dose is based on severity of the Iron Deficiency Anemia**

**Anemia**

- **Mild**: 1 tab 60 mg of elemental iron / 1 time a day / 3 months (5000 mg total)
- **Moderate**: 1 tab 60 mg of elemental iron / 2 times a day / 3 months (10000 mg total)
- **Severe**: 1 tab 60 mg of elemental iron / 3 times a day / 3 months (15000 mg total)

After correcting the anemia it is necessary to continue taking 60 mg of elemental iron plus FA 0.4 mg / day / 3 months (about 5000 mg elemental iron), to replenish iron stores.

**Ferrous Sulfate (FS)** is the first-line option; it’s the most widely used, cost-effective and has a high bioavailability. The dose of FS can increase or decrease based on the degree of anemia, and tolerance by patient, the goal is the total recommended intake of elemental iron according to the severity of the anemia, if necessary it can be administered at a greater time period.

Encourage the use of **foods that aid with iron absorption**: Vitamin C, citrus, acidic foods like tomato sauce, iron tablets without enteric coating, and intake first thing in the morning [fasting]. Avoid iron absorption inhibitors: coffee, tea, milk, cereals, soft drinks, dietary supplements or multivitamins containing calcium, zinc, manganese and copper, antacids and antibiotics such as quinolones and tetracycline.

To encourage the consumption of foods rich in (more absorbable) heme iron such as red meat, poultry, fish or liver. Non-heme iron (less absorbable) is prevalent in cereals, egg yolks, and leafy green vegetables.

**Evidence**26 - 31

**Prevention of iron deficiency anemia in menstruating women**

A systematic review was done by WHO26,29 including 21 RCT n 10,258 menstruating women from 15 countries in LAC, Asia, Africa and Europe. Women, who took intermittent iron alone or in combination with FA or other micronutrients versus no treatment or placebo, had higher concentration of Hb and ferritin and 27 % less likely to develop anemia (RR 0.73, 95% CI 0.56-0.95). In countries where this has been implemented they’ve managed to reduce the prevalence of anemia between 9 and 57 %. In regions
with high prevalence (> 30%) of intestinal parasites in addition to high prevalence of anemia (> 20%), the administration of Albendazole every 6 months, with iron and FA can eliminate (<1%) the prevalence of moderate to severe intestinal parasites in addition to reducing iron deficiency and anemia.  

The benefits of prevention, treatment and effective control of the Iron deficiency and iron deficiency anemia in non-pregnant women, improves: cognitive development, iron deposits for future pregnancy, physical and working ability, boosts immunity and reduces morbidity due to infections.  

Bibliography

Prevention and treatment of iron deficiency anemia during preconception


Interventions during pregnancy

Evaluate and achieve adequate weight gain during pregnancy using the pre pregnancy or first trimester pregnancy Body Mass Index (BMI)

Background

The prevalence of low BMI (< 18.5 kg/m²) in adult women has declined in Africa and Asia since 1980, but is still high, > 10%. In the same period the overweight (BMI ≥ 25 kg/m²) and obesity (BMI ≥ 30 kg/m²) have increased worldwide, reaching > 40% in Africa and >70% in LAC in 2008.

Overweight and obesity generate maternal-fetal adverse outcomes during pregnancy, childbirth and postpartum. Obese pregnant women compared to women with normal weight, have more risk of gestational diabetes, preeclampsia, gestational hypertension, metabolic syndrome, cardiovascular disease and congenital malformations. During labor and delivery: increased risk of maternal death, bleeding, cesarean section, infections, macrosomia, birth trauma, prematurity, fetal, neonatal and infant death, and fetal programming of chronic disease (obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease) in children, adolescents and adults, promoting the intergenerational transmission of obesity and its consequences. Children of mothers with malnutrition, overweight or obesity before pregnancy have lower cognitive performance.

Newborns with low birth weight (LBW) or preterm have independent effects on fetal and neonatal mortality. Both have increased risk of cerebral paralysis. Preterm are at risk for respiratory distress syndrome (RDS), apnea, intracranial hemorrhage, sepsis and retinopathy. The LBW (more those with fetal growth restriction) have a higher risk of hypoglycemia, hypocalcaemia, polycythemia and asphyxia.

Neonatal and post neonatal mortality is lower in infants with birth weights between 3500 and 4250 g (optimal weight), increasing up to 40 times in the LBW and up to 100 times among those with < 1500 g in the U.S, in the LAC sub region the mortality risk is much higher.

Defining nutrition: See Preconception Intervention period

The recommended weight gain during pregnancy by the Institute of Medicine (IOM) and WHO, depends on the measured pre pregnancy or first trimester of pregnancy BMI to have the best results on maternal nutritional status, the optimal birth weight and GA. The recommended weight gain is independent of age, parity, and ethnicity.
Table 9 Recommended weight gain in pregnant women according to pre pregnancy or first trimester BMI. Institute of Medicine (IOM)\textsuperscript{38,39,40,47}

<table>
<thead>
<tr>
<th>Pre pregnancy or 1\textsuperscript{st} trimester BMI</th>
<th>Recommended weight gain in pregnant women [pounds]</th>
<th>To obtain optimal birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight classification</td>
<td>BMI (Kg/m\textsuperscript{2})</td>
<td>During entire pregnancy</td>
</tr>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>28-40</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-25</td>
<td>25-35</td>
</tr>
<tr>
<td>Overweight</td>
<td>25-30</td>
<td>15-25</td>
</tr>
<tr>
<td>Obese (all)</td>
<td>≥30</td>
<td>11-20</td>
</tr>
</tbody>
</table>

* estimated weight gain during the first trimester of pregnancy of 0.5-2 kg (1.1-4.4 pounds), based on Siega Riz et al.1994, Abrams, 1995, Carmichel et al, 1997

If weight gain during pregnancy in all categories of pre pregnancy BMI / first trimester (not obese) are lower than recommended (Table 10), the risk for preterm births, SGA increases. If the weight gain is < 6 kg, the risk of neonatal, post neonatal and infant mortality increases 2-6 times.

Weight gain greater than the recommended, particularly in overweight and obese women, there is increased risk for large for gestational age [LGA] or macrosomic NB [> 4500 g], autism spectrum, and maternal complications,\textsuperscript{44,39} Adult children of obese mothers have a higher risk of obesity, hospitalizations for cardiovascular problems and increased premature death from all causas.\textsuperscript{42

**Intervention**\textsuperscript{36, 37, 41, 45, 46} (Strong recommendation, high quality evidence)

1. Counseling and monitoring of nutrition to achieve the recommended weight gain during pregnancy, according to pre pregnancy BMI or first trimester pregnancy. Ensure weight control at each antenatal visit. Educate them about the maternal, fetal, neonatal and adult risk by nutritional status.

2. Undernourished women with a balanced energy and protein supplementation (25 % of total calories as protein) reduces the incidence of SGA by 34 % (RR 0.66 , 95 % CI 0.49 to 0.89), fetal death by 40 % (RR 0.62 , 95 % CI 0.40 to 0.98)\textsuperscript{99}
Counseling points for pregnant women with overweight / obese

1. **Recommend a balanced diet** with 30% fat, 15-20% protein and 50-55% carbohydrates; diet low in fats and sugars, eat more grains, flour, cereals and pastas, fruits, vegetables, beans, lentils, oatmeal with individualized caloric intake according to the needs of the mother.

2. **Physical Activity Program** to be continued after childbirth:
Moderate physical intensity if not done before, start with 15 minutes 3 times a week and gradually increase to 30 minutes daily. It may be swimming, walking fast. If pre-pregnancy exercises were done, continue with moderate intensity.

3. **Assess the need for thrombo prophylaxis** with unfractioned heparin or low molecular weight heparin in obese mothers.

Evidence

In pregnant women with overweight / obesity diet is more effective than physical activity in reducing complications such as preeclampsia, hypertension, gestational diabetes and preterm birth, without maternal and fetal adverse effects. 45,46

In a study from Scotland 198 n 124 280 singleton births in pregnant women with BMI prior to 16 weeks GA, the maternal outcomes were compared among those who were overweight (BMI 25 - <30), obese (30 - < 40) and severely obese (≥ 40 kg / m²) and normal weight (BMI 18.5 - <25). In pregnant women with overweight, obese and severely obese, respectively, the risk was increased for: essential hypertension 87 %, RR 1.87 (1.18 - 2.96), 12 times RR 11.90 (7.18-19.72 ) and 36 times RR 36.1 (18.33-71.1), gestational Hypertension 76 % RR 1.76 (1.60-1.95), 3 times RR 2.98 (2.65-3.36) and 4 times RR 4.48 ( 3.57-5.63 ), gestational diabetes 3 times RR 3.39 (2.30-4.99), 12 times RR 11.90 (7.54-18.79), and 67 times RR 67.4 ( 37.8-20.0 ), emergency cesarean 2 times RR 1.94 ( 1.71-2.21 ), 3 times RR 3.40 (2.91-3.96) and 14 times RR 14.34 (9.38-21.94), elective cesarean 2 times RR 2.06 (1.84-2.30), 4 times RR 4.61 (4.06-5.24) and 18 times RR 17.92 (13.20-24.34) and direct relationship between increased weight and increased hospitalization and increased cost of care.

In adolescents with low socioeconomic status who become pregnant, it increases the risk of malnutrition, anemia, low birth weight, fetal restriction, increased 50% of fetal and neonatal mortality, prematurity and asphyxia. 199

In undernourished women - balanced energy and protein supplementation (25 % of total calories as protein) in a systematic review Cochrane 199 reduces the incidence of SGA infants by 34 % (RR 0.66 , 95 % CI 0.49 to 0.89), fetal death by 40 % (RR 0.62 , 95 % CI 0.40 to 0.98).

Bibliography

Evaluate and achieve adequate weight gain during pregnancy


7. **Multivitamins and folic acid in pregnant women and the prevention of NTD’s and other congenital malformations**

Definition, Background, risk factors and Evidence: See preconception period

**Interventions**\(^9,14,15\) (Strong recommendation, moderate quality evidence)

**Periconception Prevention of Neural Tube Defects with folic acid (FA) and multivitamins (MV) to prevent other birth defects**\(^9,14,15\)

It is recommended that all women who are at risk or plan to become pregnant take FA and multivitamins for 3 months before pregnancy, throughout pregnancy and throughout lactation:

**Women without risk factors for NTDs:** MV plus FA 0.8 to 1 mg / day PO, from 3 months **pre conception** up to 3 months post-conception. From 3 months post-conception throughout pregnancy and throughout lactation MV FA take 0.4 to 1 mg / day PO.

**Women with a high risk factor for NTD’s:** MV plus FA 5 mg / day PO for 3 months **pre conception** up to 3 months post-conception. From 3 months post-conception throughout pregnancy and throughout lactation MV with FA 0.4 to 1 mg / day PO.

**Daily consumption of a diet rich in FA:** green leafy vegetables (spinach, broccoli and lettuce), asparagus, avocado, fruits (oranges, lemons, bananas, melons), beans, black beans, meat (chicken, pork, fish, beef liver and kidney, tuna), tomato juice, fortified
oatmeal and wheat bran.

Evidence\textsuperscript{15, 23,25, 165, 168,169}

The pre conception MV reduced the occurrence of major congenital malformation (CM)\textsuperscript{15, 23,25} especially heart [47\%], and further ventricular septal by 74\% (Table 11). In Canada\textsuperscript{165} a meta-analysis of case-control on the use of MV showed reduction of cardiac CM by 22\% and 39\% in RCTs. Only MV can reduce CM: obstructive urinary tract, limbs and congenital pyloric stenosis.

The pre conception intake of MV (n 35 897)\textsuperscript{168,169} in women with BMI <25, is associated with risk reduction for: pre-eclampsia by almost 40\%, preterm labor 20\%, 16\% preterm infants, SGA 17\%.

A study at Griffith University, Australia \textsuperscript{221}, n 2,261 pregnancies between 2006 and 2011, The effect on the first trimester multivitamin was associated with a 67\% reduction in Pre-eclampsia risk (OR 0.33, 95\% CI: 0.14, 0.75). Stratification by BMI demonstrated a 55\% reduction in pre-eclampsia risk (OR 0.45, 95\% CI: 0.30, 0.86) in overweight (BMI: 25-29.9) and 62\% risk reduction (OR 0.38, 95\% CI: 0.16, 0.92) in Obese (BMI: ≥30) cohorts.

Recent evidence shows that the MV with FA 0.8 to 1 mg, administered in pre conception period (3 months before, 3 months after conception), can prevent: about 90\% of NTD’s vs. FA only 70\%, and 47\% of other CM including heart, 37\% preeclampsia, preterm labor 20\%, and preterm delivery 16\%. \textsuperscript{165, 168,169} (Table 12).

| Table 13 MV in Periconception period and impact on maternal-perinatal health\textsuperscript{15,23,25} |
|---------------------------------------------------|----------------|-----------------|
| **Periconception MV REDUCES**                    | RR % | RR/OR          | CI 95\%       |
| - Major CM mainly cardiac                        | 47   | 0.53           | 0.35–0.70     |
| - CM mainly ventricular                          | 74   | 0.26           | 0.09–0.72     |
| - Cardiac CM (in RCT’s Canada\textsuperscript{165} OR) | 39   | 0.61           | 0.40–0.92     |
| **MV in women with BMI< 25 REDUCES\textsuperscript{168,169}** |     |                |                |
| - Preeclampsia                                   | 37   | 0.63           | 0.42, 0.93    |
| - Preterm labor                                  | 20   | 0.80           | 0.69, 0.94    |
| - Preterm NB                                     | 16   | 0.84           | 0.73, 0.95    |
| - SGA NB                                         | 17   | 0.83           | 0.73, 0.95    |
Iron deficiency anemia [IDA] prevention and treatment in pregnant woman

Background

The average prevalence of anemia in pregnant women worldwide is 42%, from a minimum in North America of 6.1%, Europe 19, LAC 31%, and Asia 42 to a maximum in Africa of 56%. Iron deficiency (ID) is the only nutritional deficiency more prevalent and severe in the world. Iron deficiency anemia [IDA] is the most frequent deficiency affecting more than 2 billion people worldwide, with prevalence in pregnant women of 17% in rich countries and 56% (35-75%) in poor countries. Much of the total population and the majority of pregnant women in poor countries have ID without anemia, which is estimated as 2-5 times higher than the population with IDA. The ID is the cause of > 50% of the total of anemia, IDA represents the more serious stage of the ID.

Anemia in pregnancy definition

WHO Define it as a concentration of Hemoglobin (Hb)< 11 g/dL (< 110 g/l), or a hematocrit < 33% at sea level. Hb normally decreases 0.5 g/dL (5 g/l) during the second trimester of pregnancy, due to physiological hemodilution.

Severity of anemia in pregnancy. According to the WHO (Table 10) in pregnant women at sea level, Anemia measured with Hb level is:

<table>
<thead>
<tr>
<th>Severity</th>
<th>Hemoglobin (Hb) [g/dL]</th>
</tr>
</thead>
<tbody>
<tr>
<td>No anemia</td>
<td>&gt;110 g/L [≥ 11.0 g/dL]</td>
</tr>
<tr>
<td>Mild</td>
<td>100 – 109 g/L [10 – 10.9 g/dL]</td>
</tr>
<tr>
<td>Moderate</td>
<td>70 – 99 g/L [7 – 9.9 g/dL]</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;70 g/L [&lt;7 g/dL]</td>
</tr>
</tbody>
</table>

Intervention. (Strong recommendation, evidence of high quality). Administer iron as per severity of anemia for the prevention and treatment of IDA among pregnant women. The adequate treatment is dose-dependent. (Table 12)
Table 15. Prevention and Treatment of Anemia due to Iron deficiency, in women in reproductive age\textsuperscript{26,48-52} [Martínez Guillen FI]

<table>
<thead>
<tr>
<th>Severity of anemia</th>
<th>Hemoglobin (Hb) g/dL *</th>
<th>Anemia PREVENTION</th>
<th>ANEMIA TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Life course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preconception</td>
<td>11-12</td>
<td>8-&lt;11</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>10-&lt;11</td>
<td>7-&lt;10</td>
<td>&lt;7</td>
</tr>
<tr>
<td>Postnatal</td>
<td>^1-3 days</td>
<td>9-&lt;10</td>
<td>7-&lt;9</td>
</tr>
<tr>
<td>^1 week</td>
<td>9-&lt;11</td>
<td>7-&lt;9</td>
<td>&lt;7</td>
</tr>
<tr>
<td>^8 weeks</td>
<td>9-&lt;12</td>
<td>7-&lt;9</td>
<td>&lt;7</td>
</tr>
</tbody>
</table>

Replacement of iron deposits, once the IDA mild, moderate or severe is corrected: should be given one cycle of elemental iron 65 mg + FA 0.4 mg 1 tab / day / 3 months (total 5000 mg elemental iron)\textsuperscript{a}

\textsuperscript{a}In regions with high prevalence (20-30\%) of intestinal parasites, along to the I + AF, provide Albendazole 400 mg PO every 6 months in pre pregnancy; and pregnant women with moderate or severe anemia in the 2 and 3 trimester\textsuperscript{31,52}

\textsuperscript{*} hematocrit can be calculation\textsuperscript{166}: Hb (g / dL) x 3 = hematocrit %

\textsuperscript{**}In places with high prevalence of anemia (≥ 20\% of non-pregnant women)
Evidence\textsuperscript{50, 166}

A Meta-analysis\textsuperscript{50} found that the increase of maternal Hb by 10 g/L (1 g/ dL), decreased 25\% maternal mortality \{OR 0.75 (95\% CI 0.62-0.89)\} and 28\% \{OR 0.72 (95\% CI 0.65-0.81)\} perinatal mortality.

A Harvard SR\textsuperscript{166}, 48 RCTs n 17 793 and 44 cohort n 1 851 682 (almost half of both studies in low-income countries /middle income), found that anemia in the first and second trimester of pregnancy increase the risk of LBW by 29\% (OR adjusted 1.29, 1.09 - 1.53) and the preterm NB 21\% (1.21, 1.13-1.30). Prenatal iron increased the Hb 4.59 (95\% CI 3.72 - 5.46) g/l and reduced: the risk of anemia 50\%, ID 41\%, IDA 60\% and the LBW 19\% (Table 11). To increase the intake of iron per 10 mg / day, up to 66 mg / day, maternal anemia decreased 12\% (RR 0.88, 0.84-0.92, p < 0.001), the birth weight increased 15.1 g, p = 0.005 and the LBW decreased.

<table>
<thead>
<tr>
<th>Iron during pregnancy</th>
<th>REDUCES:</th>
<th>RRR %</th>
<th>RR</th>
<th>CI 95 %</th>
</tr>
</thead>
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<tr>
<td>- Risk for anemia</td>
<td>50</td>
<td>0.50</td>
<td>0.42-0.59</td>
<td></td>
</tr>
<tr>
<td>- Iron Deficiency</td>
<td>41</td>
<td>0.59</td>
<td>0.46-0.79</td>
<td></td>
</tr>
<tr>
<td>- Iron Deficiency anemia</td>
<td>60</td>
<td>0.40</td>
<td>0.26-0.60</td>
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</tr>
<tr>
<td>- LBW</td>
<td>19</td>
<td>0.81</td>
<td>0.71-0.93</td>
<td></td>
</tr>
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</table>

Bibliography

Pregnancy

Iron deficiency anemia prevention and treatment


9. PREVENTION OF PREECLAMPSIA and gestational hypertension

Background

Globally gestational hypertension affects 10% and pre-eclampsia (PE) 2-8% and in developing countries it affects 1.8 to 17% of pregnant women. WHO estimates that the incidence of PE is 7 times higher in poor countries. Studies done by WHO found that the main severe results during pregnancy [maternal deaths or missed cases] were hypertensive disorders at a rate of 30%.

A WHO Global Survey on Maternal and Perinatal Health in developing countries n 276,388 mothers and their infants was analyzed. The prevalence of pre-eclampsia/eclampsia was 4%, ranged from less than 1% in Angola to 8% in Brazil. The prevalence of PE was Africa 2%, Asia 3% y LAC 6% and outcome associated with preeclampsia/eclampsia respectively was: maternal mortality (by 100,000LB) Africa 1390, Asia 680, y LAC 50, perinatal mortality(x 1000 LB) 165, 95 y 33, preterm birth 27%, 27 y 21% y Low birth weight 24%, 34 and 24%. The highest maternal mortality was observed in Nigeria (3000 x 100,000 LB), and the highest perinatal mortality was in the Democratic Republic of Congo (220%) associated with pre-eclampsia/eclampsia.

The Risk factors to preeclampsia/eclampsia, Adjusted OR [AOR] (95% CI): chronic hypertension 8 times AOR 7.75 (95%CI 6.77–8.87), BMI ≥ 35 4 times AOR 3.90 (3.52–4.33) p<0.001, severe anemia 3 times AOR 2.98 (95%CI 2.47–3.61), cardiac or renal disease 2 times AOR 2.38 (95%CI 1.86–3.05), gestational diabetes 2 times AOR 2.00 (95%CI 1.63–2.45), maternal age ≥ 35 y 2 times AOR 1.95 (1.80–2.12) p < 0.001, nulliparity 2 times AOR 2.04 (95%CI 1.92–2.16), BMI 26 to 35 71% AOR 1.71 (1.61–1.81) p <0.001, absence of antenatal care 41%, AOR 1.41 (95%CI 1.26–1.57), maternal age 30 to 34 y, 40% AOR 1.40
(1.31–1.51) p<0.001, Education primary/ none 22% AOR1.22 (1.07–1.39) p<0.003, pyelonephritis or urinary tract infection 13% AOR 1.13 (95%CI 1.03–1.24).

The AORs for adverse maternal and perinatal outcomes of pre-eclampsia\textsuperscript{315}: Maternal death 4 times AOR 4.48 (2.99–6.69) p < 0.001, Perinatal death 2 times 1.87 (1.66–2.11) p< 0.001, Preterm birth 3 times 2.86 (2.68–3.06) p<0.001 and Low birth weight2 times 2.32 (2.16–2.50) p < 0.001.

The consequences\textsuperscript{216} in future for the women with preeclampsia are: hypertension range of risk is from RR 2 to 20 times, Ischemic heart disease 3- 4 times RR 2.80(2.20–3.70), Cerebrovascular disease 6 times RR 6.0 (5.45–6.77).

Maternal preeclampsia\textsuperscript{217} carry an increased risk of problems in adaptive functioning and mental wellbeing in the offspring seven decades later. Offspring born after pre-eclamptic pregnancies had increased odds of reporting total problems 4 times (aOR 4.00, 95% CI 1.64–9.77) and psychiatric and psychological problems 5 times (aOR 5.28, 95%CI 1.87–14.96), as (anxious/depressed, memory, thought, irritable, somatic, and psychotic problems).

\textbf{Definition}\textsuperscript{54}

\textbf{Arterial Hypertension}: systolic or diastolic or both ≥ 140/90, taken two times, the second measurement after 1 hour at rest. Allow the woman to sit for 20 minutes prior taking the BP. If the first BP measurement is ≥ 140/90 mm Hg, retake the BP after 1 hour at rest lying on the side.

\textbf{Severe Hypertension}: systolic blood pressure ≥ 160 and / or diastolic blood pressure ≥ 110 mm Hg, reconfirmed 15 minutes later.

\textbf{Significant Proteinuria}: ≥ 1 + (p< 0.01)\textsuperscript{200} urine dipstick or ≥ 300 mg protein or is if the urinary protein: creatinine ratio is greater than 30 mg/mmol in 24 hours or ≥ 500 mg/L\textsuperscript{57},\textsuperscript{200}.

\textbf{Preeclampsia}: Is a multisystem inflammatory syndrome defined as the onset of Hypertension plus proteinuria (In pregnancy > 20 weeks of gestation).\textsuperscript{57,222}
High risk for and prevention of hypertension or preeclampsia

Pregnant woman with HIGH RISK for Pre Eclampsia or hypertension\textsuperscript{55,56}

ONE of the following high risk factors is present

a. History of previous pregnancy Hypertensive Disorder, or previous pre-eclampsia, particularly when more serious or early onset before 34 weeks GA.
b. Chronic hypertension. (Before 20 weeks GA)
c. Diabetes type 1 or 2,
d. Chronic kidney disease
e. Autoimmune disease such as systemic lupus erythematos, or thrombophilia or antiphospholipid syndrome

Two or more of the following MODERATE risk factors

a. Primigravida
b. Multiple pregnancy
c. Maternal age ≥ 40 years
d. Birth interval > 10 years
e. Mother or sister History of Preeclampsia
f. BMI ≥ 35 kg/m\textsuperscript{2} at first prenatal care [PNC]
g. Urinary Tract Infection
h. Periodontal disease

Calcium for the prevention of preeclampsia or hypertension during pregnancy

a. Calcium is the most abundant mineral in the body and is essential for bone formation, muscle contraction and enzyme functioning and hormones.\textsuperscript{56}
b. WHO and FAO recommend dietary intake of 1200 mg / day of elemental calcium (3-4 cups of milk or milk products a day) during pregnancy, intake of lower dosage is considered low intake.\textsuperscript{38,41,56}

\textbf{Intervention}\textsuperscript{56-60} (Strong Recommendation of WHO, high- quality evidence)

Dose: 1.5-2 g / day of elemental calcium, divided into 3 doses at the end of meals, from 12 weeks (useful in <20 weeks) of gestation until birth, to all pregnant women in populations with low calcium intake.
In populations with low calcium intake, calcium administration to pregnant women as part of antenatal care is recommended for the prevention of hypertension, preeclampsia, maternal and neonatal morbidity and mortality, especially those with high risk of Pre Eclampsia.

Evidence

In developing countries all pregnant women irrespective of the risk for hypertension and calcium intake, calcium administration reduces the risk (Table 18) of: Preeclampsia (PE) 52 %, 41% in low risk and 82 % in high risk. It reduces severe PE by 25 %, gestational hypertension 35 % and 64 % of PE in low calcium intake, preterm births in high risk for PE patients 55%, maternal mortality / severe morbidity by 20 %. In developing countries calcium reduces: neonatal mortality from all causes by 30 %, 24% Preterm, high risk PE by 82 %.

| Table 17. Calcium to all pregnant women, in developing countries, irrespective of the risk for hypertension and calcium intake reduces the risk for: 56-60 |
|---------------------------------|-------|-------|-------|
| Calcium to All Pregnant women   | REDUCE: | RRR% | RR | CI 95 % |
| - Overall Preeclampsia          | 52    | 0.45  | 0.31 - 0.65 |
| - Preeclampsia in low intake calcium | 64    | 0.36  | 0.20 - 0.65 |
| - Preeclampsia in high risk for pre-eclampsia | 82    | 0.18  | 0.07 - 0.42 |
| - Severe Preeclampsia           | 25    | 0.75  | 0.57 - 0.98 |
| - Gestational Hypertension      | 35    | 0.65  | 0.53 - 0.81 |
| - Preterm NB                    | 24    | 0.76  | 0.60 - 0.97 |
| - Preterm NB in high risk for PE | 55    | 0.45  | 0.24 - 0.83 |
| - All causes of Neonatal Mortality | 30    | 0.70  | 0.56 - 0.88 |
| - Severe maternal Mortality / Morbidity | 20    | 0.80  | 0.65 - 0.97 |
Acetylsalicylic acid (aspirin) during pregnancy to prevent Preeclampsia / Hypertension

Interventions\(^{59,61-64}\) (Strong Recommendation, moderate to high quality evidence)

Administer low-dose acetylsalicylic acid (aspirin) 75-100 mg PO at bedtime starting at 12 weeks GA (best ≤16 weeks, useful < 20 weeks GA) until birth, to all pregnant women with high risk of pre-eclampsia or hypertension.

Evidence

Administering aspirin to pregnant women with high risk of pre-eclampsia, reduces the risk (Table 14) of: PE by 25%, gestational hypertension by 46%, and preterm newborn by 8%, SGA 10% and perinatal mortality 14%. In cases of high risk of PE the dose of > 75 mg reduces PE 36%.\(^ {59,64}\)

Initiating aspirin ≤16 weeks vs. > 16 weeks GA, provides greater reduction of: perinatal mortality by 60%, pre-eclampsia 53%, severe preeclampsia 82%, fetal growth restriction 54% and preterm newborn 65%.\(^ {65}\)

In a recent high quality systematic review for AHRQ\(^ {222}\) aspirin at 12 weeks GA in a pregnancy at risk for preeclampsia, reduce: preeclampsia 24% (RR 0.76; 0.62-0.95), the reduction was greater in doses more than 75 mg of aspirin, 42% (RR 0.58; 0.36-0.95), preterm birth 14% (RR 0.86; 0.76-0.98), IUGR 20% (RR 0.80; 0.65-0.99), perinatal mortality 20% (RR 0.81; 0.65-1.01), with no risk or harms in mother and newborn.

<table>
<thead>
<tr>
<th>Aspirin reduces:</th>
<th>RRR %</th>
<th>RR</th>
<th>IC 95 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>- PE risk in high risk women</td>
<td>25</td>
<td>0.75</td>
<td>0.66 - 0.85</td>
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<td>- PE risk in high risk PE with the use &gt; 75 mg aspirin</td>
<td>36</td>
<td>0.64</td>
<td>0.51 - 0.80</td>
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<tr>
<td>- Any adverse result in pregnant women</td>
<td>10</td>
<td>0.90</td>
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<td>- Perinatal mortality</td>
<td>14</td>
<td>0.86</td>
<td>0.76 - 0.98</td>
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<td>- SGA NB</td>
<td>10</td>
<td>0.90</td>
<td>0.83 - 0.98</td>
</tr>
<tr>
<td>- Preterm NB</td>
<td>8</td>
<td>0.92</td>
<td>0.88 - 0.97</td>
</tr>
<tr>
<td>- Ventilated NB</td>
<td>21</td>
<td>0.79</td>
<td>0.67 - 0.95</td>
</tr>
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</table>
Aspirin initiated ≤ 16 vs. > 16 GA produces MAJOR reduction\textsuperscript{65}

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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<tr>
<td>- Perinatal mortality</td>
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<td>0.41</td>
<td>0.19−0.92</td>
</tr>
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<td>- Preeclampsia</td>
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<td>- Severe preeclampsia</td>
<td>82</td>
<td>0.18</td>
<td>0.08−0.41</td>
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<td>- Preterm NB</td>
<td>65</td>
<td>0.35</td>
<td>0.22−0.57</td>
</tr>
<tr>
<td>- Fetal growth restriction</td>
<td>54</td>
<td>0.46</td>
<td>0.33−0.64</td>
</tr>
</tbody>
</table>

Bibliography

PREVENTION OF PREECLAMPSIA and gestational hypertension with Calcium and Aspirin

**Calcium**


**Aspirin**


10. **Preventing preterm birth with Progesterone**

**Background**

Preterm newborns are the main cause of morbidity, disability and perinatal mortality, neonatal and infant mortality.**66**

**Definition**

Preterm: Born before 37 completed weeks GA

**Intervention****66-68,182** *(Strong Recommendation, moderate quality evidence, for pregnant women with history of previous preterm birth. Low quality evidence for USG diagnosed short cervix)* **182**
In pregnant women, with singleton pregnancy, with history of previous spontaneous preterm birth or pregnant women that has incidental Ultrasound (not routine search) and have a short cervix (< 15 mm): manage the 17-Alpha hydroxyprogesterone caproate 250 mg IM once per week starting at 16 weeks to 37 weeks of pregnancy (the most used), or vaginal progesterone 100-400 mg / day or oral progesterone 100-200 mg / day PO.

Evidence

In singleton pregnancies, with history of spontaneous preterm birth, IM progesterone is associated with a statistical significant reduction of the risk for: perinatal mortality 60% RR 0.41 [CI 95% 0.23, 0.73], neonatal mortality 62% RR 0.38 [IC 95% 0.17, 0.87], intraventricular hemorrhage 75% RR 0.25 [IC 95% 0.08, 0.82]. IM, vaginal and Oral progesterone reduces preterm NB< 37 weeks 45% RR 0.55 [0.42, 0.74], preterm NB<34 weeks 70%, LBW 42%, assisted ventilation 60%, Necrotizing enterocolitis 70%, admission to NICU 76% and prolonged pregnancy in average 4.5 weeks.

When progesterone is indicated for short cervix diagnosed by USG it reduces preterm birth < 34 weeks 36% (RR 0.64, 95% CI 0.45, 0.90) and preterm birth< 28 weeks 41% RR 0.59, 95% CI 0.37, 0.93) and increases the hives 5 fold, it does not reduce perinatal-neonatal mortality or other results.

Bibliography

Preventing preterm birth with Progesterone


Erythromycin in Premature Rupture of Membranes (PROM) in not in labor Preterm

Background

Preterm births are the results of: 30-35% of maternal or fetal disease, spontaneous labor 40-45% and 20-30% of PROM in preterm labor. Once there are PROM in preterm pregnancy, 50% of pregnant women start labor within 24-48 hours and 70-90% within 7 days. In PROM preterm pregnancy intra-amniotic and postpartum infection occurs between 15-25%. Risk of Cerebral Palsy (CP) is inversely proportional to the gestational age (GA), is 80 times higher in NB less than 28 weeks GA. Currently, prematurity is considered the greatest risk factor for CP.

Definition

PROM is the rupture of the amniotic membranes before onset of labor, when it occurs before 37 weeks of gestational age it’s called preterm premature rupture of membrane (PROMPr).

Intervention\(^{38,69-73}\) (Strong Recommendation, high quality evidence)

All pregnant women with history of preterm, with PROM and not in labor, and without chorioamnionitis, preeclampsia, fetal distress or other contraindications to continue with the pregnancy, begin treatment before referral to higher level of resolution:

1. Erythromycin 250 mg every 6 hours for 10 days or until delivery PO, whichever comes first.
2. Apply antenatal steroid as indicated (see antenatal steroid)

Evidence.\(^{38,69,71}\)

In pregnant women with PROMPr with previous preterm birth, the use of antibiotics (Erythromycin, Penicillin) showed statistical significant reduction of: chorioamnionitis 34%, birth within 48 hours 30% and 7 days 21%, use of surfactant 17% (RR 0.83, 95% CI 0.72, 0.96), oxygen therapy 12% (RR 0.88, 95% CI 0.81 to 0.96) and neonatal sepsis. There is evidence of significant reduction (p = 0.01) for respiratory distress syndrome [RDS], intraventricular hemorrhage, enterocolitis and neonatal sepsis 39%. It is estimated that in developing countries the AB can reduce neonatal mortality for pathologies related to PROMPr births by 12% (range 3-20%), sepsis 8%, and by other complications 4%.\(^{71}\)
12. **Uterine contractility inhibitors. Oral Nifedipine (PO)**

**Background.**

In LAC approximately 8% of births are preterm (< 37 weeks GA) and in Central America it is 9 - 10%. The preterm NB contributes with > 80% of neonatal and infant mortality and the majority of the neurological sequel, mainly secondary to RDS in the NB due to pulmonary immaturity. Delaying preterm birth allows the administration of antenatal steroids for pulmonary maturation and opportune referral to a higher level of resolution for better maternal and preterm NB outcome.

**Definition.**

Uterine contractility inhibitor or tocolytics: pharmacologic agent that inhibits uterine contractions.
**Intervention**

**Nifedipine during preterm labour**\(^{38,74,75,177}\) *(Strong Recommendation, high quality evidence)*

In preterm labour < 37 weeks GA, without contraindication for the use of uterine inhibitors (preeclampsia, chorioamnionitis, fetal distress or fetal death, restriction of fetal growth or lethal CM):

**Initial dose:** Nifedipine 10 mg PO if uterine contraction continues, 10 mg every 20 minutes, 2-3 times for a total of 40 mg.

**Maintenance dose:** Nifedipine 10-20 mg PO, every 4-6 hours, based on contractions pattern, for 2-3 days.

If the blood pressure is below 110 / 70 mm Hg, do not administer Nifedipine.\(^{38}\) Caution: cardiovascular collapse is reported when used along with MgSO\(_4\).\(^{74,75}\)

**Evidence.**\(^{38,74,75,177}\)

In SR of RCT Nifedipine versus placebo and other uterine inhibitors, significantly reduces:

- 57% of deliveries within 2 days, 24% within 7 days (RR 0.76, 95% CI 0.60 - 0.97) and 17% before 34 weeks GA (RR 0.83, 0.69-0.99), the RDS 37% (RR 0.63, 0.46-0.88), necrotizing enterocolitis 79% (RR 0.21, 0.05-0.96), intraventricular hemorrhage 41% (RR 0.59, 0.36-0.98), admission and stay in NICU and less maternal adverse events 68% (RR 0.32, 0.24-0.41). The time gain before delivery is key for the administration of prenatal steroids and referral to a hospital with capacity to provide care to the preterm neonate and mom.

Nifedipine is the first line uterine inhibitor.

In a recent Cochrane\(^{223}\) systematic review 38 trial (n 3550 women). Comparing Nifedipine with placebo, no treatment or other tocolytics (betamimetics, others) showed a significant reduction in birth less than 48 hours after trial entry 70% (RR 0.30, 95% CI 0.21-0.43), fewer maternal adverse effects 64% (average RR 0.36, 95% CI 0.24-0.53), decreasing preterm 11% and very preterm birth 22% (RR 0.89, 95% CI 0.80-0.98 and RR 0.78, 95% CI 0.66-0.93); respiratory distress syndrome 36% (RR 0.64, 95% CI 0.48-0.86); necrotizing enterocolitis 80% (RR 0.21, 95% CI 0.05-0.96); intraventricular hemorrhage 50% (RR 0.53, 95% CI 0.34-0.84); neonatal jaundice (RR 0.72, 95% CI 0.57-0.92); and admissions to NICU 30% (average RR 0.74, 95% CI 0.63-0.87).

**Bibliography**

**Uterine contractility inhibitor: Nifedipine**


13. Prenatal steroids for fetal pulmonary maturation

Background

RDS is a severe complication of preterm NB and main cause of early neonatal mortality and disability. It affects up to 20% of NB with birth weight of < 2500 g and almost 70% of those with < 500 g. Also, preterm NB has a high risk of intraventricular hemorrhage and sepsis. In high income countries the majority of preterm > 25 weeks survive and in low income countries even moderate preterm NB<1500 g dies (e.g. Dhaka, capital of Bangladesh, 79% of NB<32 weeks GA died). For more than 6 decades of RCTs in women, the effect of steroids on fetal maturation [many organs and systems] was confirmed: cardiovascular, respiratory, nervous and gastrointestinal. Despite knowing that the steroids is a low cost intervention with high impact in the reduction of neonatal mortality and morbidity, in 75 countries where more than 90% of maternal, neonatal and infant deaths occur the coverage with steroids is only 10% and in LAC is still low; the coverage of steroids among pregnant women in 22 hospitals in Mexico is<20%. In these countries with low use of steroids there is an increase in the use of higher cost technologies compared to steroids such as: mechanical ventilators, application of surfactant, higher cost antibiotics without prevention and control of infections, increased hospital stay and high neonatal mortality and complications in survivors.

Between 1996 and 2008 developed countries (e.g. Switzerland) where the neonatal mortality and preterm mortality is very low and the proportion of preterm NB with birth weight <1500 g that survive without sequels is becoming higher, 72% compared with 67% (p < 0.001), the use of prenatal steroids increase (p < 0.001) from 67% in 1996 to 91% in 2008.

If universal coverage of selected interventions were to be achieved, then ≥ 84% than preterm neonatal deaths could be prevented annually, with antenatal corticosteroids and Kangaroo Mother Care having the highest impact.

Everyone has a role to play in reaching this target including government leaders, professionals, private sector, and of course families who are affected the most and whose voices have been critical for change in many of the countries with the most progress.

Definition

Preterm Labor: Labor that occurs between 20 and < 37 weeks of GA: clinically proven uterine contractions 4/20 minutes, or 6/60 min plus: rupture of membranes or intact membranes and cervical dilatation > 2 cm or intact membranes and cervical effacement > 80%, or intact membranes and cervical changes (effacement, cervix dilation), during the observation.

The threat of preterm delivery is: uterine contractions 4/20 minutes, or 6/60 min, cervical dilatation > 2 cm or intact membranes and cervical effacement > 80%.
Intervention\textsuperscript{38,76-83} (Strong Recommendation, high quality evidence)

Indications for Antenatal Steroids.

Threat of preterm delivery or preterm labor, premature rupture of membranes without chorioamnionitis, antepartum hemorrhage, hypertensive syndromes, any cause that justifies preterm delivery (fetal distress, diabetes, isoimmunization), pregnancy with elective caesarean section before 39 weeks of gestation

Treatment\textsuperscript{38,76-83}

Dexamethasone 6 mg IM every 12 hours total 4 doses or Betamethasone 12 mg IM every 24 hours total 2 doses. Threat of delivery within 24 hours, administer Dexamethasone or Betamethasone 12 mg IM every 12 hours total 2 doses.\textsuperscript{76,79,79}

Start treatment immediately after diagnosis [can be used in women with diabetes and hypertensive disorders] unless there is imminent delivery [within one hour]\textsuperscript{202} between 26 to less than 36 weeks GA,\textsuperscript{76,77,83,202} and in elective Caesarean section before 39 weeks GA.

The objective is to attain one course of total dose of 24 mg before 24-48 hours before delivery. The administration of steroids up to one hour before delivery is also useful. The optimum effect is obtained between 48 hours to 7 days after administration of the total dosage of 24 mg.

Rescue Course: 24 mg of steroids (2 courses maximum), same treatment if the previous course was administered 1-2 weeks earlier, the criteria to be indicated is met and if the delivery will occur in the following week.\textsuperscript{81,84}

Administer steroids to all pregnant women with high risk of preterm labor,\textsuperscript{202} if there is any suspected sign or symptom of preterm labor, do not wait for a confirmation of the diagnosis.

Administer a uterine inhibitor to allow the administration of a complete course of steroids.\textsuperscript{202}

Evidence\textsuperscript{38,76-83,179,180,202}

In systematic reviews of RCTs (Cochrane)\textsuperscript{76} and others\textsuperscript{77}, the antenatal corticosteroids significantly reduces (Table 15): neonatal mortality 31%, cerebroventricular hemorrhage 46%, Necrotizing enterocolitis 54%, admissions to NICU 20%, early neonatal sepsis 44% and delay in children’s development 51% and cerebral palsy 62% (0.38,0.15 - 0.80).\textsuperscript{82,180}
The use of corticosteroids are effective in PROM and hypertensive disorders during pregnancy. In high-income countries its use reduces neonatal mortality [NM] by 31%, in countries with moderate income (Brazil) it reduces NM by 53% (36-65%) and morbidity by 37%. In low income countries, where there is higher NM, the administration of corticosteroids is lower and they have small number of NICU units, here the application of corticosteroids will have greater impact in reducing neonatal morbidity and mortality.

Corticosteroids are more effective when the total dosage is administered (24 mg of dexamethasone or betamethasone) between 24-48 hours up to 7 days after the last dose administered. In suspected cases of preterm delivery within 24 hours, administer the steroids every 12 hours for the benefit of the preterm infant.

| Table 15. Prenatal steroids for fetal pulmonary maturation, reduces |
|---|---|---|
| Prenatal steroids REDUCES: | RRR % | RR | 95% IC |
| - Neonatal Mortality, high income countries | 31 | 0.69 | 0.58-0.81 |
| - Neonatal Mortality, moderate income countries | 53 | 0.47 | 0.35-0.64 |
| - Respiratory distress syndrome moderate to severe | 45 | 0.55 | 0.43-0.71 |
| - Cerebroventricular Hemorrhage | 46 | 0.54 | 0.43-0.69 |
| - Severe Cerebroventricular Hemorrhage | 72 | 0.28 | 0.16-0.50 |
| - Necrotizing Enterocolitis | 54 | 0.46 | 0.29-0.74 |
| - Neonatal Sepsis < 48 hours of life | 44 | 0.56 | 0.38-0.85 |
| - Admission to NICU | 20 | 0.80 | 0.65-0.99 |

Antenatal Dexamethasone compared with betamethasone reduces cerebroventricular hemorrhage by 56% (RR 0.44, 95% IC 0.21-0.92) and hospital stay in the NICU.

Recent studies in 22 states - USA, n 245 453 preterm NB and 4220 neonatal deaths in NICU, the specific mortality rate by GA and the comparative use or not of antenatal corticosteroids by GA. The adjusted logistic regression of confusing factors, yielded the adjusted OR with CI 95%, the antenatal steroids reduce neonatal mortality by: 44% [0.56 (0.46 - 0.67)] at 22-25 weeks GA, 34% [0.66 (0.53 - 0.83)] at 26-28 weeks, 31% [0.69 (0.55 - 0.85)] at 29-33 and 31% [0.69 (0.47 - 1.01)] at 34-36 weeks GA (late preterm).

A recent study in Australian NICU network, n 2549, exposure to a full course of corticosteroids 48 hours before birth in < 29 weeks GA reduced: 41% neonatal mortality (OR 0.59, 95% CI 0.45 - 0.76, p < 0.001), intraventricular hemorrhage 42% (OR 0.58, 95% CI 0.42 - 0.81, p = 0.001), Necrotizing enterocolitis 40% (OR 0.62, 95% CI 0.42 - 0.91, p = 0.018), the need for surfactant 60% (OR 0.41, 95% CI 0.30 - 0.57, p < 0.001) and 70% mechanical ventilation (OR 0.30, 95% CI 0.17 - 0.52, p < 0.001).
Corticosteroids are indicated in every woman at risk for preterm labor, with few exceptions, for the decrease of neonatal morbidity and mortality and the costs of health care. The use of corticosteroids for fetal maturation is a rare example of low cost technology that also improves health.

Bibliography

Prenatal steroids for fetal pulmonary maturation


14. **Periodontal disease during pregnancy**

**Background**

Approximately 40% of pregnant women have periodontal disease (PD) in developed countries, being much higher in developing countries. The maternal periodontitis is significantly associated with twice the risk of NB with LBW [< 2 500 g], preterm labor and preeclampsia. In periodontitis, the infection / inflammation process can cause placental structural changes that may lead to preeclampsia and decrease in transport of nutrients resulting in LBW and fetal tissue damage that can lead to perinatal morbidity /mortality. Periodontitis is associated to many diseases throughout the life of the woman: cardiovascular, diabetes, Alzheimer’s disease, respiratory infection, osteoporosis of the oral cavity.

**Definition**

Periodontal disease: infection-inflammatory process of the gum that may cause dental tissue damages.

**Interventions during pregnancy** (Recommendation Weak in favor, low-moderate quality evidence)

a. Health education on oral health before, during and after pregnancy

b. Assess oral health at booking clinic

c. Educate on prevention, diagnostics procedures including X Ray [protecting thyroid and abdomen] and treatment [filling and extractions are safe during pregnancy]

d. In cases of Gingivitis [edema and bleeding] to help with irritation use a salt-water mouth wash [1 teaspoon of salt in one cup of warm water], or Chlorhexidine 0.2 % mouthwash.

e. In case of vomiting or gastric reflux indicate antacids and sodium bicarbonate mouth wash (1 teaspoon sodium bicarbonate in one cup of water) neutralizes the acid.

f. Recommendations to improve oral health: limited consumption of sugary products, regular brushing of teeth, twice a year visits to Dentist.

g. Urgent referral to dentist in case of necrotizing ulcerative gingivitis, in the meanwhile administer metronidazole, or amoxicillin (metronidazole not available) or both, acetaminophen [pain] and Chlorhexidine [0.2 %] mouth wash 3 times / day.
**Evidence**

In SR of RTC non-surgical treatment including Chlorhexidine for periodontal disease during pregnancy, significantly reduces LBW preterm.\(^87\)

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15. **Urinary Tract Infections [UTI’s]**

**Background**

UTI’s during pregnancy affects up to 20% of women in developing countries can lead to PROM, preterm labor and delivery, chorioamnionitis, neonatal infection, pre-Eclampsia LBW and preterm NB.\(^38,90-92\)

UTI’s classification: asymptomatic (asymptomatic bacteriuria), or symptomatic: cystitis and pyelonephritis. Asymptomatic bacteriuria range from 2-10%, if not treated, 30- 50% progress to symptomatic UTI and pyelonephritis 1-2 %.\(^90\)
Definition

Asymptomatic bacteriuria means no symptoms or signs of UTI, and presence of at least 100,000 CFU/mL of urine, of a single pathogen, from a clean midstream urine sample.

Best diagnostic for asymptomatic or symptomatic UTI is urine culture done between 12-16 weeks GA, or first prenatal care.\(^\text{38}\)

Other diagnostic method is the use of urine with positive nitrites and leukocytes esterase. Other findings are proteinuria y hematuria.\(^\text{96,91}\)

Signs and symptoms of UTI’s:

**Pyelonephritis:** bacteriuria plus: fever, chills, nauseas, vomiting, and loin tenderness positive.

**Cystitis:** bacteriuria plus: frequency, urgency, dysuria, piuria and there could be hematuria, low abdominal or suprapubic pain.\(^\text{96}\)

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**Intervention**\(^\text{38,90-97,183}\) *(Strong Recommendation, moderate to high quality Evidence)*

In asymptomatic bacteriuria or Cystitis, nitrofurantoin 100 mg/ PO 2 times/day taken with food or Cephalexin 500 mg PO 2-3 times/day, or Cephadroxil 500 mg 2 times/day. Treatment duration is 7 days for asymptomatic bacteriuria and 10 days for Cystitis.

Persistent asymptomatic bacteriuria or asymptomatic bacteriuria that develops symptoms or recurrent UTI (3 UTI in last 12 months or 2 UTI’s in last 6 months)\(^\text{13}\) or persistent UTI or concomitant renal lytiasis, treat with nitrofurantoin 100 mg 4 times/day or Cephalexin 1 g every 6-8 hours or Cephadroxil 1 g 2 times/day, for 10-14 days, followed by Prophylaxis for the rest of the pregnancy: nitrofurantoin 100 mg o Cephalexin 125mg o Cephaclor 250 mg, at bedtime.

Acute pyelonephritis: (prior urine culture) treat with Cephtriaxone 1 g every 24 h, or every 8-12 h in severe infections -IM or IV en 5 minutes-, for 10-14 days. Treatment resistance [no clinical response in 72 hours] change to gentamycin at 3-5 mg/Kg/day IV every 8 hours, (or gentamycin 5 mg/Kg/ day every 24 hours)\(^\text{184}\) for 10 days plus ampicillin 1-2 g IV every 6 hours for 10-14 days. After two days afebrile, change to PO high dose cephalosporin as mentioned in persistent asymptomatic bacteriuria for 14 days.

In a high quality prospective study on pregnant women with pyelonephritis due to E Coli, the most frequent cause, half show resistance to ampicillin in the urine culture, after treatment with ampicillin and gentamicin (synergy), clinical maternal and perinatal outcomes were not different between resistant and non-resistant to ampicillin, this scheme is still clinically useful.\(^\text{183}\)
Evidence

Treated asymptomatic bacteriuria <20 weeks (early) vs. >20 weeks GA (late) for 7 days significantly REDUCES maternal-neonatal complications.  

Pyelonephritis is significantly associated (p <0.001) with: restricted uterine growth, abruptio placentae, low Apgar and preterm birth, and can be reduced with appropriate treatment.

One dose of gentamycin every 24 hours in pregnant women, has low quality evidence and there is no justification for high doses.

Bibliography

Urinary Tract Infections


16. Elimination of Congenital Syphilis

Background

Syphilis is a sexually transmitted infection, a serious public health problem globally, it is estimated that each year there are 12 million new infections, and more than 2 million among pregnant women. Worldwide the Latin America and the Caribbean (LAC) presents the highest maternal syphilis infection rate, 3.9% between 1997-2003, which resulted in nearly 0.5 million pregnant women with syphilis and up to more than 340,000 cases of congenital syphilis each year. Most times the infection is transmitted to the fetus between 16-28 weeks GA and is fatal in 30-50% of the cases.98

There is the "initiative for the Elimination of the transmission of mother to child HIV and congenital syphilis in Latin America and Caribbean" by 2015.

Definition98

Maternal or gestational syphilis. Any woman during pregnancy and postpartum period or with recent spontaneous abortion with Clinical Evidence of: chancroid, syphilitic rosella or flat wart or serological syphilis.

Congenital Syphilis, any of the following scenarios:

a. Maternal syphilis without appropriate treatment with fetal or Neonatal death, or spontaneous abortion

b. Child with titers four times [2 dilutions] higher than maternal titers [e.g. mother 1:4, child 1:16]

c. Child with suggestive clinical manifestations of congenital syphilis and positive serological test irrespective of titers level.

d. Gestational or placental product with Evidence of infection due to T. Pallidum in Histological studies.

Syphilis elimination: reduce congenital syphilis ≤ 0.5 cases per 1000 LB (includes fetal deaths).98

Serological diagnosis criteria: all reactive serological treponemic or non treponemic (RPR) is considered positive irrespective of titer level. From an epidemiological and programmatic perspective all positive serology is a presumptive diagnosis (possible), ensure early treatment.98
**Intervention.**

Intervention: \(^{98-102}\) (Strong Recommendation, high quality Evidence)

Screen all pregnant women [serology] for syphilis in the first prenatal visit; if it is negative repeat in the third trimester. A third screening is done upon admission before childbirth or in the postnatal period prior to discharge [in case of imminent delivery or fully dilated upon admission]. If the test for syphilis is positive mother and her partner should receive the treatment.

Adequate treatment for syphilis: penicillin received at least one month before delivery and immediately after receiving the result [preferably rapid test] in primary care level.

Syphilis treatment [primary, secondary and early latent syphilis] benzathine benzyl penicillin 2.4 million IU, IM.

In late latent syphilis or latent syphilis of unknown duration, the total dose is 7.2 million IU of penicillin benzathine penicillin, in doses of 2.4 million IM every week.

**Treating congenital syphilis**

**Congenital syphilis**

**Clinical Evidence of congenital Syphilis**

a. Asymptomatic born to mother with syphilis and did not receive appropriate treatment

b. Asymptomatic born to mother with syphilis with adequate treatment with titers 4 times higher than maternal titers

c. Asymptomatic born to mother with syphilis treated adequately, with no titers to measure against maternal titers.

d. Asymptomatic born to mother with syphilis and: non-documented treatment, no reduction of titers, no syphilis testing [RPR] or positive re-infection

For any of the above, complete assessment, treat with crystalline penicillin 50,000 IU/ Kg every 12 hours (100,000 IU/ Kg / day) during the first 7 days of life, continuing with 50,000 IU/ Kg / every 8 hours (150,000 IU/ Kg/ day) up to 10-14 days. If neurologic manifestations, treat for up to 14 days, Procaine benzylpenicillin50,000 IU/ Kg / day [daily dose] for 10-14 days.

Asymptomatic children of mothers with syphilis treated adequately with titles equal or lower than the maternal titer should receive a dose of Benzathine penicillin of 50,000 IU / Kg, independent of the treatment received by the mother and without further testing.
Evidence

Late screening for syphilis and late antenatal checks (third trimester) compared to the first or second trimester, increases the adverse outcomes and congenital syphilis between 2 and 4 times (OR 2.24, 95% CI 1.28, 3.93). The early detection and treatment of maternal syphilis can significantly reduce: 97% congenital syphilis, 82% fetal death, 64% preterm births and 80% neonatal mortality, perinatal morbidity and mortality.

Bibliography

Elimination of Congenital Syphilis


17. Labor induction > 41 weeks GA

Background

In France prolonged pregnancy is 15-20%, and post-term pregnancy varies in Europe and the USA between 0.5% - 10%. Some risk factors for post term pregnancy are: obesity, parity, maternal age > 30 years. Both the mother and children have more adverse effects when the pregnancy is ≥ 41 weeks GA, significantly increasing the risk of neonatal and post neonatal mortality.
**Definition**

Term pregnancy is between 37 to <42 completed weeks GA, prolonged pregnancy is ≥ 41 weeks and post term is ≥42 weeks GA.

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**Intervention** *(Strong recommendation, high quality Evidence)*

Induce labor in women with ≥ 41 weeks GA with no contraindication for labor induction [e.g. multiple pregnancy or polyhydramnios] with oxytocin (mainly used) or prostaglandins, reduces the risk of perinatal mortality, cesarean section and meconium aspiration syndrome.

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**Evidence** *(103,104,105)*

Compared with expectant management, having a policy on labor induction in pregnancies at ≥ 41 weeks GA, is associated with reduction of: 70% perinatal mortality from all causes (RR 0.31, 95% CI 0.12 - 0.88), 50% meconium aspiration syndrome (RR 0.50, 95% CI 0.34-0.73), macrosomia and cesarean section.

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**Bibliography** *(Labor induction > 41 weeks GA)*


Postnatal Interventions

18. Prevention of birth asphyxia

Background

The birth asphyxia prevalence rate per 1000 births is lower in rich countries: 0.4 Japan, 2 Great Britain, 5 Brazil, 25 Bosnia-Herzegovina and 46 in Tanzania.174

- Study of cohort (n 11,482), University of Bristol171, United Kingdom, 3 groups of newborns was evaluated:

NB requiring cardiopulmonary resuscitation [CPR], asymptomatic after and did not need more neonatal care

NB with CPR who developed hypoxic-ischemic encephalopathy

Reference group without CPR and further neonatal care

Between 8-11 years of age the capacity for was measured: attention, language, memory and need for educational support. The newborns that they did not needed CPR had Apgar average 9 at 1 min, and 9-10 at 5 minutes, the neonates with asymptomatic CPR the 1 minute Apgar was on average 5 (range 4-6) and the 5-minute Apgar score 9 (range 8-9), those of hypoxic-ischemic encephalopathy 1 minute Apgar average of 4 (range 3-6), the 5 minute Apgar score 8 (range 6-9) (p<0.001). Asymptomatic children after CPR had similar results to infants without CPR, but those who developed ischemic hypoxic encephalopathy had all tests significantly decreased and needed six times more educational support (OR 6.24, 1.52 - 26.43).

These previous studies and others174 indicate that the severe birth asphyxia causes high neonatal mortality, neurodegenerative diseases, mental retardation and epilepsy. But even the slight asphyxia is associated to "lesions with minimal brain damage": attention-deficit, hyperactivity, but also to schizophrenia and psychotic syndromes. Asphyxia and the re-oxygenation can enhance the development of neuroses-generative diseases, diabetes 2, and cancer174.

Cohort studies in Denmark and Sweden with 14 years of follow-up study, n > 5 million, in 8087 children with cancer (1.6 per 1000), comparing children with Apgar score 9-10 at minute 5, those with **Apgar score 0-5 had 50% greater risk of cancer** (RR adjusts 1.46, 95% CI 1.15 - 1.89) and more than 4 times the risk for Wilms tumor (RR 4.33(95% CI 2.42 to 7.73).175
Definition. WHO ICD-10 Code, last version made emphasis on:

Birth asphyxia should not be used with only APGAR criteria, without mentioning asphyxia or other respiratory problem.

Severe birth asphyxia

Respiration absent or gasping, hear rate [HR] or pulse <100 per minute, static or decreasing, pallor and tone absent.

Asphyxia within minute 1 Apgar of 0 - 3. White asphyxia.

Mild to moderate birth asphyxia:

Normal respiration not achieved within one minute, HR ≥100/minute, muscle tone and some response to stimuli.

Asphyxia within minute 1 Apgar of 4 - 7. Blue asphyxia.

In the WHO basic guideline on neonatal resuscitation asphyxia is defined as failure at birth to initiate and sustain breathing.

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Preventing birth asphyxia (currently called "affections related to delivery") and its consequences, can be approached in three levels. (Strong recommendation, high quality Evidence)

1. **Primary Prevention before and during labor and delivery.**
   - Preventing and promptly treating risk factors and fetal morbidities (Table 20).
   - Improving access and quality of obstetric care, mainly in the high risk pregnancy. Emergency obstetric care may reduce neonatal mortality due to asphyxia by 85% and 50% the hypoxic ischemic encephalopathy (HIE).

2. **Secondary prevention of morbidity, mortality and long term sequel** in children with Intrapartum asphyxia or develops HIE. Immediate resuscitation measures by trained personnel in cases of birth asphyxia can reduce the neonatal mortality by 30% plus the neurological sequel. Helping Babies Breathe [HBB], promoted by the AAP and the Neonatal Alliance is successfully applied in > 50 countries, the criteria used to initiate CPR are children that do not cry after drying at birth, clearing airway and stimuli.

3. **Tertiary prevention**: improving early detection and treatment for children with disabilities, early stimulation and support for families.

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**Background**

Approximately 10% of NB requires some assistance to start breathing at birth and < 1% extensive resuscitation. Globally, about 25% of all neonatal deaths are caused by asphyxia at birth. The effective neonatal resuscitation at birth can avoid much of these deaths.

**Definition**

NRP is a procedure to save the life of the NB, which takes place when breathing or heartbeat has stopped.
Neonatal Cardio-pulmonary Resuscitation STEPS

A  (Air) permeable airway, initial stabilization steps (heat source, head positioning, clear airways, drying and stimulation)

B  (Breathing) initiates breathing. Ventilation

C  (Circulation), thoracic compression (cardiac massage)

D  (Drug) Medications or volume expansion

Each step is to be completed in 30 seconds, in sequential order, and at the end of each step ensure the cycle of evaluation, decision and action is completed to continue with the next steps. Assess based on: breathing, heart rate, starting with breathing.

The 2010 publication on NRP by the American Heart Association and the American Academy of Pediatrics there has been some additions from the WHO guidelines on basic neonatal resuscitation.\textsuperscript{109, 110}
BIRTH

Term NB? Breathing or crying? Good Tone?

NO

Heat source, clear airway, stimulation

30 SEC

Apnea? gasping, ? HR <100/min?

NO

Difficulty breathing? Persistent Cyanosis?

YES

PPV, Consider monitoring SPO2

60 SEC

HR < 100/min?

YES

Ensure appropriate ventilation, ETT?

NO

HR < 60/min?

YES

Chest compression & PPV

NO

HR < 60/min?

YES

Epinephrine IV

Consider monitoring SPO2 and CPAP

Post Resuscitation Care

Routine Care- Dry, Heat, Airway Continuous Evaluation

Neonatal Resuscitation Algorithm 107
Recommendation 1

In term NB or preterm NB that does not require positive pressure ventilation, the umbilical cord SHOULD NOT be clamped before the first minute of life [best after pulsation ceased, approximately 3 minutes]. [Strong recommendation, based on moderate / high quality Evidence, it reduces the need for blood transfusion and increases iron storage]

Recommendation 2

NB not breathing spontaneously after being dried stimulate by rubbing the back 2-3 times before clamping the cord and initiate positive pressure ventilation. (Weak recommendation, Evidence: missing in humans, only in animals. This practice should be continued). In preterm and term NB requiring PPV, do not clamp the umbilical cord before 1 minute after birth and better until pulsation ceased.

Recommendation 3

NB with clear amniotic liquor, breathing spontaneously after birth, do not need mouth and nose aspiration. (Strong recommendation, high quality Evidence)

In NB with clear amniotic fluid, not breathing after drying and rubbed back 2-3 times, the suction of the mouth and nose must be before the PPV, only if it is filled with secretions. (Weak recommendation, based on consensus)

Evidence

Healthy children with oral or nasal suction at birth are associated with desaturation of oxygen (high Evidence) and low Apgar (low Evidence).

(Weak recommendation, based on consensus). Evidence: Healthy children with oral or nasal suction at birth is associated with desaturation of oxygen (high Evidence) and low

Recommendation 4

In the presence of meconium amniotic fluid, the suction of nose - mouth in the Intrapartum (head out of the vagina), is not recommended. (Strong recommendation, low-quality Evidence).

Recommendation 5

NB with meconium amniotic fluid that starts breathing spontaneously, DO NOT performs tracheal suction (strong recommendation). DO NOT suction mouth or nose (weak recommendation, based on consensus).
Evidence

Moderate or low quality evidence; tracheal suction, do not reduce mortality, or meconium aspiration syndrome in vigorous NB.

In NB with meconium stained liquor that does not start breathing spontaneously, the suction of the mouth and trachea should be performed before the PPV. (Recommendation weak, based on low quality Evidence) –

Recommendation 6

In places where mechanical equipment to generate negative pressure for the suction of secretions is not available and a NB requires aspiration, a bulb (single-use or easy to clean) is preferable to suction with a trap in which the provider generates suction extraction. (Weak recommendation).

Recommendation 7

In NB that does not start breathing after dried and stimulation, the PPV must start within one minute after birth. (Strong recommendation). Although the Evidence is of low quality and based on observational studies.

If there are trained personnel apply PPV with bag and mask, before cord clamping, place the NB between the legs of the mother or on a table at the level of the maternal pelvis. The resuscitation of the newborn with intact umbilical cord allows placental transfusion, which provides most necessary blood volume and oxygen.\textsuperscript{204, 205}

Recent research shows that early clamping of the UC leads to rapid decrease of the heart preload that can lead to bradycardia, decreased cerebral perfusion. The PPV prior to the cord clamping improves markedly the cardiovascular function by increase in pulmonary blood flow, which stabilizes the cerebral hemodynamics transition, which may be a physiological reason why delayed cord clamping reduces the risk of intraventricular bleeding.\textsuperscript{205} If there is no skilled staff, and the NB require PPV you can do immediate cord clamping and start the PPV at the reanimation table.\textsuperscript{204}

Recommendation 8

Term and preterm NB > 32 weeks GA, requiring PPV, ventilation must be started with air. (Strong recommendation, moderate quality Evidence that reduces mortality and increased start time spontaneous breathing). The available Evidence suggests that the majority of the NB ≤ 32 weeks GA can be resuscitated with PPV using air; some need Fraction of Inspired Oxygen ($\text{FiO}_2$) at 30% or more according to the evolution and the Oxygen Saturation ($\text{SpO}_2$).

Recommendation 9

NB requiring PPV, ventilation must be done with self-inflating bag and facial mask (Weak recommendation, poor quality Evidence). In situations of none availability of auto inflatable bag, the PPV can be done via mouth-tube and mask or mouth to mask.
Recommendation 10

NB requiring PPV, ventilation must be initiated with facial mask. (Strong recommendation, limited Evidence with others such as nasal cannula)

Recommendation 11

In NB requiring PPV, the adequacy of ventilation should be evaluated by measuring the HR after 60 seconds of ventilation with visible thoracic movements. The HR is the first indicator of recovery. (Strong recommendation, based on low quality Evidence, observational studies in humans and animals)

Recommendation 12

In NB that does not start breathing within 1 minute after birth; the priority should be to provide adequate ventilation rather than chest completion. [Strong recommendation, in observational studies, low quality]

Evidence

Ventilation is the most effective intervention for asphyxia in the newborn. When a second trained reanimator is present, and the NB continues with HR < 60 / minute, after 1 minute of PPV, start chest compressions besides the PPV.

Recommendation 13

In NB with HR not detectable after 10 minutes of effective ventilation, resuscitation must end. (Strong recommendation, based on Evidence of unlikely benefit for the NB).

Evidence

The neonatal resuscitation reduces: early neonatal mortality in facility 40 % (RR0.62, 95% CI 0.41-0.94), Immediate newborn assessment, drying, and stimulation 10% (range 0-25 %), Basic neonatal resuscitation (facility) 30% (95% CI 16 - 41%) Basic neonatal resuscitation (community) 20 % (Range 10-50%)

Bibliography

Asphyxia and Neonatal Cardio-pulmonary Resuscitation


20. **Cord clamping when pulsation ceased**

**Background**

There is controversy on cord clamping, in most of the maternity units it is done early at 3-15 seconds, in recent years RCTs have shown the advantage of delayed cord clamping, allowing placenta fetal transfusion of 20-30 mL / Kg in 2-3 minutes, improving iron deposits and reducing anemia in children, a public health problem in many of the developing countries.  

**Definition.**

Early cord clamping is usually before 60 seconds; delayed cord clamping is done after the first 60 seconds or when the pulsation ceased [approximately 3 minutes].

**Intervention: delayed cord clamping**

*Delayed clamping of the umbilical cord (between 1-3 minutes after birth or when pulsation ceased)* is recommended in all births, while simultaneously start newborn essential care. (Strong recommendation, moderate quality Evidence)

The early clamping of the umbilical cord (1 minute after birth) is not recommended unless the newborn is asphyxiated, cannot be resuscitated with intact umbilical cord and need to be moved immediately to the resuscitation table. (Strong recommendation, moderate quality evidence)

In NB born by caesarean section, dry the NB, clothe and place on maternal thighs (or at a level slightly lower than the placenta), while waiting for pulsation to cease. If there is a need for early cord clamping to attend the NB, "milk" the umbilical cord 5 times, from placenta end towards the NB, for placenta transfusion, with similar results to delayed cord clamping.
Evidence.\textsuperscript{110-112,204,208}

Cord clamping in term NB, delayed and early cord clamping showed no difference in the reduction of maternal and neonatal mortality and morbidity. Delayed cord clamping resulted in increased birth weight [101 g], Hb concentration at 24-48 hours, iron deposit between 3-6 months and phototherapy due to jaundice.

Delayed Cord clamping in preterm NB (24-36 weeks GA) reduces: need for transfusions due to anemia, intraventricular hemorrhage (all grades) and necrotizing enterocolitis\textsuperscript{112}.

Bibliography


21. Exclusive breastfeeding within the first hour of life

Background

The importance of breastfeeding \([\text{BF}]\) for the child nutrition status, prevention of chronic diseases and the reduction of neonatal and under five morbidity and mortality is well established. A 2003 study on the impact of BF on neonatal and child survival, were done in 42 countries where 90\% of under five deaths occur.\textsuperscript{204} Among all interventions studied Exclusive breastfeeding \([\text{EBF}]\) in the first six months, followed by BF from 6 - 11 months of age was the most effective intervention to prevent 22\% of neonatal mortality and 13\% of under five deaths.\textsuperscript{19,204}
Definition

BF have a nutritional, immunological, psycho emotional and logical development components that contribute to the optimal development and growth of children, facilitates a positive maternal and child relationship, health benefits are short and long term for the mother, NB, infants and children. The EB is based only on breast milk, including expressed breast milk, does not include intake of any other liquids [e.g. water] or food during the first 6 months of life.

Interventions

The ten steps for successful BF are the mostly promoted interventions by the UN agencies [WHO and UNICEF] and other organizations worldwide. (http://whqlibdoc.who.int/publications/9241561300.pdf.)

All facilities offering birthing services should have the following:

1. Have a written policy on BF and communicated to the health care workers
2. Train all HCW in its implementation
3. Inform all pregnant women of the benefits of EBF and BF
4. Help mothers to initiate BF within the first 30 minutes after birth
5. Teach the mother how to breastfeeding even if separated from the child
6. Give the NB only breast milk, any other liquid only with medical indications
7. Rooming in 24 hours.
8. Teach BF on demand
9. Do not use bottle-feeding or teats
10. Promote support groups and refer mother to a BF counselor upon discharge

Peripartum BF in mothers and healthy term NB (strong Recommendation, high quality Evidence)

Prenatal

All pregnant women should receive education about the benefits and management of BF, to allow an informed decision about BF. The NB must receive EBF for the first 6 months, continue breastfeeding up to 2 years or more, with the introduction of complementary foods from 6 months of age, education must include benefits of EBF for the mother and the NB from the 1st half hour of birth, potential side effects of drugs during labor.
Labor and delivery

Having a companion at birth (e.g. partner, mother, and health personnel) during labor and delivery reduces: hospital stay, use of pain medications, surgery and the start and duration of BF. High-dose Intrapartum fentanyl can prevent BF.

Immediate Postpartum

The healthy NB, vaginal delivery or caesarean section, must be placed immediately - after birth near the mother breasts in skin to skin contact, until the first feeding is completed. The NB can be dried; Apgar evaluated and initiate physical examination, together with his mother. Early and extensive skin to skin contact increases the duration of the BF. Delay the following procedures, after the 1st hour of life: weight, length, vitamin K application, ocular prophylaxis, improves the mother-NB interaction.

Mother - NB, rooming in [together 24 hours], improves the opportunity of attachment and optimal start of BF. The Evidence indicates that the mother gets the same amount and quality of sleep. Make sure the staff documents the wellbeing and proper nutrition of the NB. C-section mothers require greater support and a trained staff should document the BF at least every 8-12 hours after delivery until discharge. The breastfed NB can be fed 8-12 times in 24 hours.

Do not provide supplements to breastfed NB, unless medically indicated. Adverse effects of supplementation are: delayed lacto -genesis, breast engorgement, altered normal intestinal flora, increases allergies and delayed correct attachment.

No bottles or teat to breastfed NB, it reduces EBF and BF.

In general acute infections, fever without diagnosis and common postpartum infections in the mother are not contraindications for BF, if such diseases can be easily controlled. BF in untreated active Tuberculosis, herpes simplex lesions in breasts and in the case of mothers with HIV (developed countries) is not recommended.

Exclusive breastfeeding starting within the first hour of life.***WHO Recommendations***. (Strong recommendation, high -moderate quality evidence)

Guidelines for optimal feeding of LBW NB (< 2500 g) and very LBW (< 1500 g) in low and middle income countries (Strong Recommendation, high quality Evidence)

Recommendation 1

NB with LBW (<2500 g) and VLBW (<1500 g), must be fed with its own mother's milk. LBW NB must be put to the breast as soon as possible after birth, within half an hour of life (strong Recommendation, moderate Evidence reduces severe morbidity, and low Evidence in reducing mortality and improved neuron development)
Recommendation 2

NB with LBW and VLBW that cannot be breastfed with milk from its mother, must be fed with donated breast milk. (Strong recommendation, where there are milk banks, high-quality Evidence in reducing severe morbidity)

Recommendation 3

The LBW and VLBW NB that cannot be fed with its mother's milk or donated human milk must be fed with standard infant formula, up to 6 months. (Weak in favor recommendation, relevant for areas with limited resources, based on Evidence there is lack of significant benefits of pre-term infant formulas in the reduction of mortality rates, long term growth and neural development)

VLBW NB that cannot be breastfed with milk from their mother or donated breast milk must be fed with formula for pre-term if they are not gaining weight despite an adequate infant formula feeding standard. (Weak in favor, relevant recommendation for limited resource settings)

Recommendation 4

The VLBW NB that are fed on their mother's milk or donated human milk, do not need to receive bovine milk-based human milk fortifiers. The VLBW NB, which does not increase weight despite adequate breastfeeding, should receive human milk fortifiers, preferably based on human milk. (Weak in favor, relevant recommendation for limited resource settings, quality of the Evidence very low and high costs).

Recommendation 5

The VLBW NB with EBF or BF from their mother or donated human milk must receive supplements of 400-1000 IU / day PO of vitamin D, from the first days of life (7th day) until 6 months of age (weak recommendation in favor, Evidence of poor quality)

Recommendation 6

The VLBW NB breastfed by their mother or with donated human milk should get 120-140 mg / kg / day of calcium and phosphorus 60-90 mg/kg/day during the first months of life. (Weak recommendation in favor, low quality Evidence).

Recommendation 7

The preterm NB, if they are not exclusive breastfeeding, should receive 10 mL/Kg/day of breast milk, starting from the first day of life, with increase of up to 30 mL / kg / day, completing the rest of their fluids and calories requirements via IV. (Weak, recommendation for limited resource settings).

Recommendation 8

VLBW NB requiring EGT for feeding should receive it in intermittent bolus. (Weak Recommendation in favor)
Evidence

Educational programs during pregnancy and the support during childbirth and postpartum period promoting BF improve the initiation and continuation of BF at short and long term (p< 0.05) (high quality Evidence)\textsuperscript{116,189}

Effects of BF on neonatal mortality

In a RCT\textsuperscript{120} n 22 838, NB partially breastfed in comparison with EBF showed 77 % risk of death (RR 1.77 95% IC 1.32–2.39). The adjusted neonatal mortality (weight, GA, others) was 41% higher (RR 1.41; 95% IC 1.08-1.86) when BF starts >24 h compared with < 24 h of age.\textsuperscript{120} all causes of neonatal mortality can reduce by 19% and 8% if EBF begins within the 1st hour or 1st day of life respectively.\textsuperscript{120}

In another RCT\textsuperscript{119}, double-blind, placebo controlled, with n 11, 316 showed a significant dose response relationship in the increase of the risk of neonatal mortality with increasing delay in the onset of breastfeeding 1 hour to 7 days. (Table 17). Adjusted with all confounders factors (age, sex, weight, etc.), compared with the start 1 hour of life, the delay in the onset of BF 1 hour to 1 day of life, increased neonatal mortality 50%, day 2 is increased by 2.5 times, day 3 increases 3 times, 3 days increases 4 times, all statistically significant (p \textless 0.0001). Newborns who received on day 1 of life, different food than breast milk before settling the BF 63% increased risk of neonatal mortality (OR 1.63; 95% IC 1.09-2.45; p0.017). The partial BF vs. EBF increases the risk of neonatal death 4.5 times (4.51 OR 95% CI 2.38-8.55).

Neonatal mortality can be reduced by 22% and 16% respectively if all NB are EBF in the 1st hour or in the 1st day of life.\textsuperscript{119}

<table>
<thead>
<tr>
<th>Begins breastfeeding</th>
<th>No. of neonates</th>
<th>No. Deaths (% risk) (^a)</th>
<th>OR to 1 (95% IC)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within one hour</td>
<td>4763 (43)</td>
<td>34 (0.7)</td>
<td>1</td>
</tr>
<tr>
<td>Between one hour and end of the day</td>
<td>3105 (28)</td>
<td>36 (1.2)</td>
<td>1.45 (0.90, 2.35)</td>
</tr>
<tr>
<td>Day 2</td>
<td>2138 (20)</td>
<td>48 (2.3)</td>
<td>2.70 (1.70,4.30)</td>
</tr>
<tr>
<td>Day 3</td>
<td>797 (7.3)</td>
<td>21 (2.6)</td>
<td>3.01 (1.70, 5.38)</td>
</tr>
<tr>
<td>After day 3</td>
<td>144 (1.3)</td>
<td>6 (4.2)</td>
<td>4.42 (1.76,11.09)</td>
</tr>
<tr>
<td>Total</td>
<td>10 947 (100)</td>
<td>145 (1.3)</td>
<td></td>
</tr>
</tbody>
</table>

\(a\) % of risk: No. of deaths / No. exposed by category. \(b\) OR A: Odds Ratio adjusted by: sex, GA, weight, CM, health at birth, maternal health, age, parity, education, others
**Effects of BF on child morbidity**

**High quality Evidence (causal).** BF reduces: intestinal infections, upper and lower respiratory infections, otitis media, acute lymphoblastic leukemia (24% in EBF 6 m), childhood obesity and SIDS.

Evidence in development: improves cognitive development, reduces: atopia, asthma and other, pediatric cancer.

**Effects of BF on women**

High quality Evidence (causal). BF helps with postpartum weight loss, amenorrhea, reduce risk for breast cancer.

Evidence in development. BF reduces ovarian cancer; type 2 diabetes, and cardiovascular disease.

A Meta-Análisis on 6 cohorts n 273,961 and 10,842 cases, BF reduce Diabetes type 2 in longer duration of breastfeeding (> 6 m) 32 % RR 0.68 ,95% IC: 0.57-0.82. and for every incremental year in BF total duration it reduces by 9 % RR 0.91 (95% IC 0.86-0.96).

**Short term effects of BF on child mortality**

Diarrhea. The protecting effect of BF on diarrhea is higher in children ≤ 6 months, but also in older children. BF reduces the severity of diarrhea, hospitalization by 72 % and mortality by 77 %. Globally, BF reduces la diarrhea morbidity by 31 %, RR 0.69 (95% IC 0.49-0.96)

Upper and lower respiratory infections the protecting effect of BF for respiratory infections, is not modified by age, it reduces the risk for hospitalization by 57 % RR 0.43 (95% IC 0.33-0.55)] and mortality 70 % RR 0.30 (95 % IC 0.16- 0.56).

**Long term effects of BF on children**

The meta-analysis of the effect of BF on the overweight/obesity, blood pressure, diabetes and intelligence suggests that the benefits are greater for children and adolescents and less for adults, suggesting a gradual dilution of the effect over time.

**Diabetes** In the combined analysis there is a significant reduction of 34%, but the studies were heterogeneous.

**Overweight /obesity** BF is associated with a reduction of 24% overweight/obesity, although in high quality studies the reduction was 12%.

**Intelligence:** Strong Evidence of causal effect of BF on improves IQ.

**Benefits of BF for premature NB**

BF reduces late sepsis, necrotizing enterocolitis, retinopathy of the premature, rehospitalizations in the first year of life, improved neural development. Additionally
reduces: metabolic syndrome, blood pressure, and low density lipoprotein, leptin and insulin resistance during adolescence.

**Evidence of BF effects on the mother**

**Return to pre-pregnancy** weight in 1-2 years postpartum in women providing EBF vs. no BF is statistically significant in: multiparas with BMI < 25 (P=0.02) and for primipara with BMI ≥ de 25 (P=0.04).\textsuperscript{191}

In women with no history of gestational diabetes, type 2 diabetes decreases statistically significant (p 0.001) for each year of EBF, by 40%, RR 0.60 (95% CI 0.54-0.73), and for each year of total lactation decreases 24% RR 0.76 (95% CI 0.71-0.81).\textsuperscript{191}

Moderate quality studies report association of not BF or short period of BF (6 weeks) with increase in postpartum depression in 52 % (OR 1.52, 95% CI 1.12-2.06).\textsuperscript{191}

A Systematic review, of 3 meta-analysis, n 95 655 cases y 179 510 controls, BF for 12 months or beyond versus NO BF reduces breast cancer con histologic diagnosis by 30% OR 0.72 (95% CI 0.65-0.80).\textsuperscript{191}

A meta-analysis, of mothers who breastfed for 12 or more months versus those that did not breastfeed, the risk of ovarian cancer reduced by 28% (OR0.72, 95% CI 0.54 - 0.97).\textsuperscript{191}

**Bibliography**

**Exclusive breastfeeding**


Mother Kangaroo Method [MKM]

Background

LBW NB (2500 g) is the largest contributor of child mortality: 60-80% of neonatal mortality, two-thirds of child mortality and are an important factor for diseases in adulthood. Conventional care of LBW NB or care for premature NB is costly and scarce in developing countries. MKM is a very useful alternative demonstrated in developing countries for the care of the LBW NB or premature.124, 127 The MKM allow parents to take care of the preterm NB and infant / LBW NB and promotes family health in this critical moment. The MKM in developing countries for LBW NB has shown to reduce: mortality, severe diseases, infections and hospital stay even in developed countries, is beneficial for Premature NB. In the preterm it improves: thermal and cardiorespiratory stability, the duration of quiet sleep, lactation, neurodevelopmental and modulates the response to pain.127

Definition.124, 125

In this method the mother is the "incubator" (skin to skin contact) to maintain the NB temperature, source of food with BF and stimulation for the premature or with low weight NB, while the NB is mature enough for extra uterine life under similar conditions to the term NB.
MKM[^124-127,220]. [Strong recommendation, high quality Evidence]

MKM is the care for premature NB or LBW trough skin to skin contact with the mother. It’s an efficacious method and easy to apply promoting the health and wellbeing of term and preterm NB.

Main characteristics

a. **Mother-baby Early skin to skin contact, continuous and prolonged**

b. **Exclusive breastfeeding (ideal); starts in hospital and continues at home**

c. **Small babies can be sent home earlier**

d. **At home the mothers will need adequate support and follow up**

e. **It's an amicable method and efficacious avoiding crowded NICU's**

When to begin the MKM

The NB needs to be in stable condition: breathing spontaneously, without additional oxygen. The ability to feed (suck and swallow) does not constitute a fundamental requirement; you can start with feeding tube. As soon as the infant begins its recovery, discuss the desirability of MKM with the mother.

Arrange with the mother a moment that is conducive for both mother and baby. The first session is important and requires total attention. Ask the mother to use light, loose clothing. They are accommodated in a private and warm room for small babies. It is advisable to bring the partner or a companion of her choice if she wishes. This contributes to the mother to feel supported and tranquil.

While the mother holds her baby, describe the steps that comprise the MKM, do a demonstration and allow her to practice. It will emphasize that skin-to-skin contact is essential to keep the baby warm and to protect them from diseases.

**Kangaroo position**

Place the baby between the mother’s breasts, in vertical position, with the chest of the NB (skin to skin) in contact with the mother’s chest. Hold the NB with a Strip. Turn the head to one side, slightly extended. The top of the Strip will be just below the baby’s ear. The head is in slight extension position (avoid flexion and hyperextension) to keep the airways open and allow mother-child visual contact.

The hip is flexed and legs extended in a frog posture; the arms must also be flexed.

Show the mother how to position the NB.
Explain to the mother that BF in kangaroo position is ok. In fact, MKM care facilitates BF. In addition, by holding the baby stimulates the breast milk production.

Caring for the NB in kangaroo position

Babies can receive most of the necessary care, including feeds while in kangaroo position. Interrupt the skin-to-skin contact for: changing diapers, hygiene and care of the umbilical cord and clinical evaluation, according to the hospital plan or when it is necessary.

The daily bath is neither necessary nor recommended. If local customs dictate, this should be short and at a temperature of around 37 ° c immediately after the method is concluded, dry the baby thoroughly, wrap the baby in warm clothes and return him to the Kangaroo position as soon as possible.

During the day, the mother carrying a baby in Kangaroo position can do what she pleases: walking, standing, sitting, or participate in recreational or educational activities. Such activities can alleviate boredom make her stay at the hospital easier. Frequent Hand washing must be emphasized. The mother sleeps better with the NB in kangaroo position or in a recline or semi-recline position, around 15 degrees from horizontal.

Daily and total duration of kangaroo position

Daily duration

Skin-to-skin contact should begin gradually not less than 60 minutes and increasing, to become continuous as much as possible, day and night, and stopped only to change diapers. When the mother is separated from the baby, they should be well wrapped up in a heated crib, away from all current air and covered with a blanket.

Total duration

Skin-to-skin contact may continue, at first instance in the institution and later at home, while the baby is comfortable, usually reaching around 40 weeks GA or 2500 grams. At this time the MKM is no longer necessary, the NB begins to squirm to denote being uncomfortable, pulls out his limbs, cries and complains every time that the mother attempted to return to kangaroo position. When this occurs it is safe to recommend the mother to gradually abandon the MKM. EBF must continue. The mother go back to skin to skin contact occasionally, after bathing the baby, during a cold night or when the baby needs comforting.

Evidence

In the meta-analysis of the first systematic review of MKM, most of Studies were RCTs, in NB <2000 g at birth in hospitals in low- and middle-income countries, it showed a statistically significant reduction of: neonatal mortality 51% (RR 0.49, 95% CI 0.29-0.82) and 66% severe morbidity (RR 0.34, 95% CI 0.17-0.65).
A systematic review of RCTs Cochrane\textsuperscript{124}, MKM intermittent or continuous in LBW NB (<2500g), at the time of discharge at 40-41 weeks GA age, was associated with a statistically significant reduction of: mortality risk by 40% (RR 0.60, 95% CI 0.39-0.93), 55% nosocomial sepsis (RR 0.45, 95% CI 0.27-0.76), hypothermia 66% (RR 0.34(95% CI 0.17 - 0.67) and hospital stay.

The MMC improves physical growth and development in children with < 2500 g at birth. In an India controlled-trial\textsuperscript{220} mothers with their children n 500 with weights < 2500 g were studied, in groups of 5, the 3 newborns with lower weights were assigned to the MKM up to 40 weeks of corrected gestational age or weight of 2500 g and the other 2 infants were assigned to standard care. All newborns were exclusively breastfed up to 6 months. The anthropometry measurement (weight, size, cephalic, chest and arm perimeter) was taken at birth, at 40 corrected gestational weeks, 3, 6, 9 and 12 months. The group of children from the MKM, even though they had lower birth weights of they've achieved similar physical growth and mental development parameters than the control group at 40 weeks of corrected age, but at 3, 6, 9 and 12 months of age, they outperformed the control group. There was a statistical significant difference in all parameters [p<0.001].

MKM is also beneficial for premature NB even in high-income countries. There is more: thermal and cardiorespiratory stability, neurological development, organization and duration of quiet sleep, breastfeeding, and modulation of the response to pain, they are more alert and responds better to pain stimuli and are less irritable.\textsuperscript{127}

**Bibliography**

**Mother Kangaroo Method**


23. Congenital syphilis elimination

Congenital syphilis, any of the following scenarios:\(^{98}\)

Maternal syphilis without appropriate treatment with fetal or Neonatal death, or spontaneous abortion

Child with titers four times [2 dilutions] higher than maternal titers [e.g. mother 1:4, child 1:16]

Child with suggestive clinical manifestations of congenital syphilis and positive serological test irrespective of titers level

Gestational or placental product with Evidence of infection due to \(T.\) Pallidum in histological studies.

**Background** and bibliography See syphilis during pregnancy.

**Syphilis elimination** Reduce congenital syphilis to \(\leq 0.5\) cases /1000 NB (fetal deaths included).\(^{98}\)

**Serological diagnosis criteria** all reactive serological treponemic or non treponemic (RPR) is considered positive irrespective of titer level. From an epidemiological and programmatic perspective all positive serology is a presumptive diagnosis (possible) to ensure early treatment.\(^{98}\)

**Intervention**\(^{98,102}\) (Strong Recommendation, high quality Evidence)

Treatment of children with congenital syphilis

**Congenital syphilis in children:**

a. Clinical evidence of congenital Syphilis

b. Asymptomatic born to mother with syphilis and did not receive appropriate treatment

c. Asymptomatic born to mother with syphilis with adequate treatment with titers 4 times higher than maternal titers

d. Asymptomatic born to mother with syphilis treated adequately, with no titers to measure against maternal titers.

e. Asymptomatic born to mother with syphilis and: non-documentated treatment, no reduction of titers, no syphilis testing [RPR] or positive re-infection
These children should have complete evaluation, treated with penicillin Crystalline 50,000 IU / Kg every 12 hours (100,000 IU / Kg / day) the first 7 days of life, continuing with 50,000 IU / Kg / every 8 hours (150,000 IU / Kg / day) up to 10-14 days. In the case of neurological manifestations the therapy must be for 14 days. Alternatively if neurosyphilis is discarded penicillin procaine 50,000 IU / Kg / day a daily dose 10-14 days. Asymptomatic children of mothers with syphilis treated adequately with titles of RPR equal or lower than his mother should receive a dose of Benzathine penicillin of 50,000 IU / Kg, independent of the treatment received by the mother and no further testing is required.

Evidence

Screening for syphilis late in pregnancy (third trimester) compared to doing it early at first or second trimester, increases adverse outcomes in general and congenital syphilis between 2 and 4 times (OR 2.24, 95% CI 1.28, 3.93)\textsuperscript{100} The detection and early treatment of maternal syphilis can significantly reduce: 97% fetal death, 82% congenital syphilis 64% preterm births and 80% neonatal mortality, perinatal morbidity and mortality \textsuperscript{101,102}

24. Neonatal Hypothermia, consequences and prevention

Background

Hypothermia is very common, in NB in hospital; the prevalence varies between 32 and 85% and in children born at home between 11 to 92%, even in tropical environments. Hypothermia is a high risk for neonatal morbidity and contributes substantially in neonatal mortality overall, as comorbidity of sepsis, asphyxia and premature NB. Neonatal hypothermia is associated with increased risk of infection, coagulation defects, acidosis, delayed fetal-neonatal circulatory adaptation, hyaline membrane disease, and cerebral hemorrhage, increased consumption of oxygen and mortality rates.\textsuperscript{133}

The lack of thermal protection is not quantified, is underestimated and it's a great challenge for neonatal survival in developing countries.\textsuperscript{129,130} Thermal protection is a series of measures at birth and in the first days of life to ensure normal temperature to the NB between 36.5 - 37.50 C (97.7-99.50 F)\textsuperscript{128}

A recent study in the community in 213,616 axillary temperature at 23240 NB, neonatal mortality was significantly increased in hypothermia: mild 70\% (RR 1.70; 95% CI 1.23-2.35), moderate 4.6 times (RR 4.66; 95% CI 3.47-6.24) and severe 23 times (RR 23.36 95% IC 4.31-126.70).\textsuperscript{130}

Definition
Hypothermia - WHO

Normal temperature in NB: 36.5-37.5°C.

Hypothermia: when the NB temperature is 36.5°C (97.7°F).
- Mild hypothermia: 36-36.5°C (96.8-97.7°F)
- Moderate hypothermia: 32-36.0°C (89.6-96.8°F)
- Severe hypothermia < 32°C (<89.6°F)

Interventions to prevent neonatal Hypothermia

A. To implement the thermal protection of the NB in the hospital or at home, from birth and the first few days of life, apply the 10 steps recommended by WHO, the "hot chain" steps:

1. **Warm delivery room** Maintain delivery Room clean and warm [temperature between 25-28°C]. The NB may be lost temperature in the first 10-20 minutes [2-4°C].

2. **Dry the NB immediately** Dry with dry, warm, towels while the NB is on a warm surface e.g. maternal abdomen or thorax (skin to skin contact).

3. **Skin to skin contact** Effective method to prevent loss of heat in term or Pre term NB. After drying The NB placed on the mother's abdomen or thorax, which should be clean and dry, skin to skin contact, then cover with the same dry sheet used by the mother.

4. **Early breastfeeding:** Start BF within half hour of life and encourage BF on demand or every 2-3 hours while the BF is established. A proper intake of breast milk is essential to provide: heat, heat that generates heat to the body, nutrients and antibodies. Also skin to skin contact transfers heat to the NB.

5. **Postpone the bath** and weight. Bathing of the NB must be after 24 hour of life. Bathing him immediately after birth causes hypothermia and is not necessary. Blood, meconium and vernix are cleaned when drying the NB. The weight may be delayed several hours after birth when the NB is stable.

6. **Clothe the NB and dress the bed appropriately** depending on the room temperature. The NB needs one or two layers of sheets more than adults and a CAP, as 25% of the loss of heat in the NB is through uncovered head.

7. **Keep the mother and newborn together** Children born in hospital or at home, must remain with the mother 24 hours a day (accommodation - together), preferable in the same bed, in a room with temperature not less than 25°C.
Rooming-in promotes breastfeeding, avoid hypothermia and hospital-acquired infections.

8. **Maintain the hot temperature during transport** If the NB require transfer to another room or hospital, it is very important to keep the NB within normal temperature.

9. **Warm reanimation** It is very important to keep the NB warm (normal temperature) during resuscitation, because the newborn with asphyxia does not produce heat efficiently and can suffer hypothermia.

10. **Awareness-raising and training** The HCW, institutional and at community level who attends childbirth and the NB and the family require to be trained in hot chain 10 steps.

B. NB≥37 weeks GA or birth weight≥ 2500 g place them in a none medical plastic bag (Polyethylene) or cover the body and extremities with plastic without drying and continue with the caring of the NB. \[^{132}\]

C. A NB of 26- 36 weeks GA and / or birth weight 1000- 2500 g, place in non-medical plastic bag[low cost Polyethylene]or cover body and extremities with plastic, after drying quickly on the maternal abdomen and cord clamping. One hour later remove plastic bag if the NB temperature is normal. \[^{133}\]

---

**Evidence** \[^{131}-^{133}\]

In NB < 28 weeks GA applying wrappers or plastic bags reduces the loss of heat in 0.70 °C 95% CI 0.45-0.91, the plastic caps were effective in reducing the loss of heat in 0.80° C in < 29 weeks GA.

Skin to skin contact compared with conventional incubators, reduces hypothermia 91% (RR 0.09; 95% CI 0.01, 0.64).

Thermal mattress reduces 70% (RR 0.30; 95% CI 0.11-0.83) hypothermia admission to NICU in NB < 1500 g.

NB ≥ 37 weeks GA or birth weight ≥2500g placed inside plastic bag vs. standard care at birth, had lower risk of hypothermia 24% (RR 0.76, 95% CI 0.60-0.96, p = 0.026) and more axillary temperature (36.4 ± 0.5 ° C vs. 36.2 ± 0.7 ° C)(, p < 0.001) 1 hour after birth, for limited resources settings. \[^{132}\]

NB between 26-36 weeks GA and/or birth weights between 1000- 2500 g, place in a non-medical plastic bag [polyethylene of low cost] vs. standard care, had most likely a normal temperature within one hour of life. \[^{133}\]

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**Bibliography**
Neonatal Hypothermia


25. Chlorhexidine and umbilical cord to prevent omphalitis and neonatal sepsis

Background

Of the 3.3 million annual neonatal deaths that occur in the world, more than 30% are caused by infections, many of which begin in the navel (omphalitis). Many of these bacteria come from birth canal, the environment in which the delivery occurs, and from HCW hands.

Definition
Umbilical infection can be localized in the umbilical cord (Omphalitis) or it may enter the bloodstream, turning it into a systemic infection (neonatal sepsis) ¹³⁴

**Intervention.**¹¹⁰,¹³⁴-¹³⁶ *(Strong recommendation, high quality Evidence)*

Applying Chlorhexidine 4% aqueous solution or gel on the umbilical cord for 7 days on NB born at home or hospitals, where there is high neonatal mortality (≥ 30 x 1000 LB) and in countries with limited resources.

**Evidence of Chlorhexidine 4% and umbilical cord**

**Neonatal mortality**

The meta-analysis of 3 high quality, community-based RCTs, with n = 44,818, comparing Chlorhexidine and leaving the umbilical cord dry, significantly reduces the risk of neonatal mortality 17% (RR 0.83, 95% CI 0.74-0.94) ¹³⁴

In other RCT the use of Chlorhexidine in the community significantly reduced neonatal mortality 38% (RR 0.62, 95% CI 0.45-0.85; p = 0.003) ¹³⁵

In systematic review Cochrane ¹³⁶ Chlorhexidine applied at community level n 54,624, showed reduction of neonatal mortality from any cause by 23% (RR 0.77,95% CI 0.63-0.94

**Effect on Sepsis and omphalitis**

The use of Chlorhexidine at community level reduced the Omphalitis by 32-75% (RR 0.25, 95% CI 0.12 - 0.53), the reduction was greater for severe Omphalitis when the application of Chlorhexidine was carried out within 24 hours of birth. ¹³⁴

In RCTs Chlorhexidine reduced Omphalitis by 42% (RR 0.58, 95% CI 0.41-0.82; p = 0.002). ¹³⁵

In a systematic review from Cochrane ¹³⁶ Chlorhexidine applied in the community reduced Omphalitis between 27% to 56%, depending on the severity of the infection.

**Bibliography**

Chlorhexidine and umbilical cord to prevent omphalitis and neonatal sepsis


135. Soofi S, Cousens S, Imdad A, Bhutto N, Ali N, Bhutta ZA. Topical application of chlorhexi-dine to neonatal umbilical cords for prevention of omphalitis and neonatal mortality in a rural district of Pakistan: a community-based, cluster-
26. Vitamin D in breastfed neonates for the prevention of Vitamin D deficiency and rickets

Background

Currently, it is clear that Vitamin D (Vit D) participates in the regulation of the metabolism, cell growth, and immunity. Vit D deficiency is associated with osteoporosis, diabetes, asthma, rheumatoid arthritis, multiple sclerosis, resistance to TB and pathogenesis of specific cancers (moderate quality Evidence). \(^{137}\)

Women during pregnancy and lactation period, more in developing countries, is often deficient in Vit D and their children premature or term children with EBF are at risk for deficiency of Vit D and rickets, if not supplemented with Vitamin D early. \(^{137, 138}\)

Rickets varies in children less than 3 years: 9% in Nigeria, 10% in Turkey, 15% in Greece and 66% in the Tibet. \(^{139}\)

Definition

The plasma levels of Vitamin D [25 (OH) D] are defined as: optimum between 75-225 nmol/L (30-90 ng/mL), insufficient 25-75 nmol/L (10-30 ng/mL), deficient <25 nmol/L [<10 ng/mL]. \(^{137}\) The optimum level is defined as parathyroid hormone production level and calcium intestinal reabsorption is stable. The levels >225nmol/L can be associated to hyperkalemia and deposits of calcium in the tissues.

Intervention. \(^{137, 139-142}\) \textbf{(Strong recommendation, high quality Evidence)}

The American Academy of Pediatrics\(^{140}\) and others (Institute of Medicine of the National Academy, Canadian and European Pediatrics Society)\(^{141}\) recommended that to prevent Vitamin D deficiency and rickets in children and adolescents, that the term NB, preterm or NB with birth weight < 2500 g with exclusive or partial BF, should be given 400 IU / day, Vitamin D orally beginning between 3-5 days of life until the first year of life, when the child receives that amount of Vit D in foods.

Evidence
In RCTs with n 1700, Cochrane and others\textsuperscript{139} administering Vitamin D compared to no intervention in term NB decreased Nutritional Rickets by 24% (RR 0.76 (95% CI 0.61 - 0.95) to 96% ()) RR 0.04, 95% CI 0 - 0.71).

In randomized double-blind trial\textsuperscript{218} the prevalence of Vitamin D deficiency (VDD) in the 800-IU group was significantly lower 4% than in the 400-IU group at 40 weeks (RR: 0.57;95% CI 0.37–0.88) and at 3 months corrected age 64% (RR 0.36; 95% CI 0.14–0.90). Bone mineral content and bone mineral density (p=0.26) were not different between the 2 groups.

**Bibliography**

Vitamin D in breastfed neonates for the prevention of Vitamin D deficiency


Vitamin A supplementation during neonatal period

Background

Vitamin A deficiency (Vit A) is a public health problem estimated to affect 19 million pregnant women and 190 million children in preschool age, and mostly those living in poverty. Small children have greater needs for vitamin A, due to rapid growth and their need to combat infections, but they do have scarce reserve at birth, and depends on external sources of which breast milk is the most important.

In Low and Middle Income countries, infants may receive insufficient amount of vitamin A in breast milk because of maternal malnutrition. Vitamin A deficiency may cause visual impairment (night blindness), anemia, reduced resistance to infections with increased risk for illnesses and death during childhood such as measles, diarrhea and pneumonia. Evidence shows that Vit A may prevent deaths due to all causes and specific mortality rates in children 6-59 months, although there is controversy on its effects in children below six months of age.

Definition

Vitamin A deficiency

Vitamin A deficiency is a public health problem if there is:

a) Night blindness (Table 18)

<table>
<thead>
<tr>
<th>Public Health Importance</th>
<th>Night Blindness</th>
<th>Serum Vit A Deficiency, serum retinol &lt; 0.70 μmol/L (&lt;20 μg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>Children 24-71 months</td>
<td>Pregnant women</td>
</tr>
<tr>
<td>- Mild</td>
<td>&gt; 0% - &lt; 1%</td>
<td></td>
</tr>
<tr>
<td>- Moderate</td>
<td>≥ 1% - &lt; 5%</td>
<td>≥ 5%</td>
</tr>
<tr>
<td>- Severe</td>
<td>&gt; 5%</td>
<td></td>
</tr>
</tbody>
</table>

b) Serum Vit A Deficiency, serum retinol <0.70 μmol/L (<20 μg/dl). The public health classification is done utilizing the proportion of preschool children or pregnant women with vitamin A deficiency: (Table 21)

Mild: ≥2 % - < 10 %
Moderate: ≥ 10 % - < 20 %
Severe: ≥ 20 %.
Intervention.144-152 (Weak in favor recommendation, mild to moderate evidence)

Provide Vitamin A 50,000 IU PO to term or preterm NB with LBW in the first 48-72 hours of life in communities where children < 5y, pregnant women or lactating mothers suffer from: malnutrition, anemia, frequent infections, poor nutritious food, in NB with LBW or preterm or with eye problems [xerophthalmia, night blindness > 1%] or where Vit A deficiency is greater than 20% among pregnant women.152

Dosage in NB with BW ≤ 1500 g or ≤ 32 weeks GA, Vitamin A 5000 IU, IM 3 times / week x 4 weeks.149

Initiate EBF on demand within first 30 minutes of life.

Evidence

In SR of 21 RCT144 at the level of the community in developing countries, the administration of Vitamin A in the neonatal period reduced infant mortality due to all causes, to the 6th month of age by 12% (RR 0.88, 95% CI 0.79-0.98). The supplementation of Vitamin A to children 6-59 months, reduced mortality from all causes by 25% (RR 0.75, 95% CI 0.64-0.88) and diarrhea mortality rate by 30% [RR 0.70; 95% CI 0.58-0.86].

In a RCT145, in one rural community of India, n 11,619 children (target Group for Vit A, 31% with BW < 2500 g), the administration of Vitamin A in the first 48 hours of life, reduced the mortality rate in the first 6 months of life by 23% (RR 0.77, 95% CI 0.62-0.96). The reduction in mortality was 52% (RR 0.48, 0.33-0.69) in NB with < 2000 g, 37% in NB with < 2500g, significant reduction in diarrhea lethality by 50% (RR 0.50 [0.27, 0.90] and fever by 40% (RR 0.60 [0.40, 0.88]) 145, 146

In double blind RCT147, in rural Bangladesh, n 15,937 (54% with LBW) oral Vit A was administered at home [50,000 IU] to NB average age of 7 hours of life and were followed up for 2.5 years, there was a significant reduction in the risk of death from all causes by 15% [RR 0.85, 1.00-0.73;] (P< 0.045)] to the 6th month of life. The protection was without distinction by sex, gestational age and weight at birth, with the likelihood of survival beyond the 6th month of life, significantly higher (P < 0.037) in the group receiving Vit A.

In a RCT148 in a Guinea-Bissau community, n 4,345 children were followed for 3 years. All children received Vit A at 1 year of age. Among those that had received the neonatal Vitamin A vs placebo, the mortality in children 1-3 years of age, was significantly lower by 46% (RR 0.54, 0.31-0.94), greater reduction observed in females, 63% [RR: 0.37, 0.16-0.86]. The decrease of 85% mortality [RR 0.15, 0.03-0.67], was higher in girls who also received Vit A in the neonatal period, during vaccination campaigns and during the study.

In a Cochrane SR of RCT149 the neonatal supplementation of Vit A vs. NB control ≤ 1500 g or ≤ 32 weeks GA, reduces mortality or requirement of oxygen at 1 month of age by 7% (RR 0.93, 95% CI 0.88-0.99) and requirement of oxygen at 36 weeks GA by 13% (RR 0.87, 95% CI 0.77-0.98).
A Cochrane SR of RCT's 151 446 neonates, was done in developing countries. When analyzing term NB with neonatal Vit A in 3 studies the neonatal mortality fell by the 6th month by 18 %(RR 0.82; 95% CI 0.68-0.99), when all 5 studies were included the mortality had a statistically significant decreased by 14% (RR 0.86; 95% CI 0.77 - 0.97).

Bibliography

Vitamin A supplementation during neonatal period


Iron for the prevention of iron deficiency and iron deficiency anemia in neonates

Background
Recent investigations supports that iron deficiency [ID] without anemia and iron deficiency anemia [IDA] can seriously cause irreversible neurological development and behavioral impairment hence, the need to eliminate ID. ID is the single nutrient efficiency most frequent in developing countries, worldwide.  

Definition
Iron deficiency: state of insufficient iron to maintain physiological functions. Iron deficiency Anemia: anemia due to iron deficiency.

Neonatal Intervention to prevent iron deficiency and iron deficiency anemia (Strong recommendation, high quality Evidence)

Breastfed Preterm(< 37 weeks GA), or LBW ( < 2500 g) newborns should receive elemental iron supplementation at 2 mg/ kg/ day orally, starting at one month up to 12 months of age.

Newborn with birth weight <1500 g, administer elemental iron at 2-4 mg/ kg/ day/ PO, starting at 14 days- 1 month, up to 12-15 months of age to prevention deficiency.

Term NB EBF or partially breastfed, should receive elemental iron at 1 mg/ kg/ day/ PO starting at the 4th month of age, until iron rich complementary feeding is provided.

Formula fed children do not need iron supplementation during the first 12 months of life. Use of whole milk formula is recommended after one year of age.
Evidence

In CochraneSR\textsuperscript{154} evidences suggest that children supplemented with iron have higher level of Hb, greater iron reserve and lower risk for developing iron deficiency anemia.

In the SR of 15 RCT, preterm or LBW children supplemented with iron PO or fortified formulas, significantly increased the levels of iron (Hb, hematocrit, serum ferritin), lowering the levels of ID and IDA and behavioral problems, without adverse events.\textsuperscript{155,160}

In RCT\textsuperscript{155} supplementation to children with birth weight between 2000 -< 2500 g, exclusive or partially breastfed, between the 6\textsuperscript{th} week - 6\textsuperscript{th} month with iron PO significantly reduced iron deficiency at 6 months of age [dose-dependent](P <0.001), anemia iron deficiency(P<0.004), it also reduces the risk of behavioral problems at 3.5 years of age.\textsuperscript{158}

Bibliography

Iron for the prevention of iron deficiency and iron deficiency anemia in neonates


Bibliography

Various


194. Cheslack-Postava K, Liu K, Bearman PS. California Sibling Births Closely Spaced Pregnancies Are Associated With Increased Odds of Autism in California Sibling Births. *Pediatrics* 2011;127;246; originally published online January 10, 2011;


Nutrition during pregnancy

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Food Group</th>
<th>Daily intake</th>
<th>Example of portions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Calories</td>
<td>Cereals</td>
<td>6 ounces</td>
<td>1 slice of bread, 1 cup ready to eat cereal or ½ cup rice, pasta or cooked cereal could be considered 1 ounce of cereal food group</td>
</tr>
<tr>
<td>2. Proteins</td>
<td>Meat and Beans</td>
<td>5 - 6 ounces</td>
<td>2-3 ounces of meat: beef, poultry or fish. ½ cup cooked beans, 1 egg, 2 teaspoon peanut butter, ½ cup nuts or seeds, equals 1 ounce “meat and beans”.</td>
</tr>
<tr>
<td>3. Calcium</td>
<td>Milk</td>
<td>3 cups</td>
<td>1 cup milk or yogurt, 1 ½ ounces of natural cheese, or 2 ounces processed cheese, equals 1 cup “milk”. Sardines.</td>
</tr>
<tr>
<td>4. Vitamins and Minerals</td>
<td>Fruits</td>
<td>1½ - 2 cups</td>
<td>1 cup fruit or 100% natural juice or ½ cup dried fruits = 1 cup of “fruits”</td>
</tr>
<tr>
<td>5. Minerals</td>
<td>Vegetables</td>
<td>2½ cups</td>
<td>1 cup raw, cooked or juiced vegetables, or 2 cups raw green leafy vegetables = 1 cup “vegetables”.</td>
</tr>
</tbody>
</table>
Annex 2 Life Course: Preconception

The objective is Safe Pregnancy: assessment of the future pregnant woman and her partner by a skilled HCW that can identify and modify risk factors or pathologies to have a healthy pregnancy and child.

<table>
<thead>
<tr>
<th>Preconception Interventions</th>
<th>Quality of evidence</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5 years Pregnancy spacing</td>
<td>High quality evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Assess nutritional status using BMI - under nutrition, overweight, obesity-</td>
<td>High quality evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Folic acid for the prevention of NTD's</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>MV to prevent CM - non NTD's-</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Prevention of IDA</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Treat IDA</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
</tbody>
</table>

Annex 3 Life Course: Pregnancy (Antenatal)

The objective is to continue with interventions for a safe pregnancy: early assessment of the pregnant woman and partner as early as possible [no later than first trimester] by a skilled HCW to identify and modify risk factors and pathologies and achieve a healthy pregnancy and healthy child.

<table>
<thead>
<tr>
<th>Interventions - pregnancy</th>
<th>Quality of evidence</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess weight gain during pregnancy using pre pregnancy or first trimester pregnancy BMI - Under nutrition, overweight, obesity -</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Folic Acid to prevent NTD's</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>MV to prevent CM other than NTD's</td>
<td>High quality Evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Anemia treatment</td>
<td>High quality evidence</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Intervention</td>
<td>Quality of Evidence</td>
<td>Recommendation</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Prevention of Pre-Eclampsia and gestational hypertension: Calcium</td>
<td>High quality Evidence [^{56-60}]</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Prevention of Pre-Eclampsia and gestational hypertension: Acetylsalicylic acid (aspirin) during pregnancy</td>
<td>Moderate to high quality evidence [^{59,61-64}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Prevention of preterm birth – progesterone</td>
<td>Moderate quality evidence [^{100-106}] for pregnant women with history of previous preterm birth. Low quality evidence for USG diagnosed short cervix [^{182}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Erythromycin in preterm PROM</td>
<td>High quality Evidence [^{38,69-73}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Uterine contractility inhibition: Nifedipine</td>
<td>High quality evidence [^{38,74,75,177}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Antenatal Corticosteroids for fetal pulmonary maturation</td>
<td>High quality evidence [^{38,76-83,179,180,202}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Periodontal disease</td>
<td>Low- moderate quality evidence [^{38,85-89}]</td>
<td>Recommendation Weak in favor</td>
</tr>
<tr>
<td>Urinary Tract Infections</td>
<td>Moderate to high quality Evidence [^{38,90-97,183}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>STI’s – Syphilis</td>
<td>High quality Evidence [^{98-102}]</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Labor Induction &gt; 41 weeks GA</td>
<td>High quality evidence [^{103-105}]</td>
<td>Strong recommendation</td>
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</table>
### Annex 4Life Course: Postnatal

<table>
<thead>
<tr>
<th>Postnatal Interventions</th>
<th>Quality of evidence</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of Birth Asphyxia</td>
<td>High quality evidence&lt;sup&gt;107&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Cardiopulmonary reanimation</td>
<td>High- moderate quality Evidence&lt;sup&gt;107-110,219&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Cord clamping until pulsation ceased</td>
<td>High quality Evidence&lt;sup&gt;110-112,209,210&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>BF within the first hour of life</td>
<td>High -moderate quality evidence&lt;sup&gt;114-123&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Kangaroo mother Method</td>
<td>High quality Evidence&lt;sup&gt;1,124-127,220&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Neonatal Hypothermia prevention</td>
<td>High quality Evidence&lt;sup&gt;110,123-125&lt;/sup&gt;</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Cure of umbilical stump with Chlorhexidine</td>
<td>High quality Evidence&lt;sup&gt;110,154-156&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Congenital syphilis elimination</td>
<td>High quality Evidence&lt;sup&gt;90-102&lt;/sup&gt;</td>
<td>Strong Recommendation</td>
</tr>
<tr>
<td>Vitamin D in breastfed neonates for the prevention of Vitamin D deficiency</td>
<td>High quality Evidence&lt;sup&gt;97,139,242&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Vitamin A during neonatal period</td>
<td>Mild to moderate quality evidence&lt;sup&gt;144-152&lt;/sup&gt;</td>
<td>Weak in favor recommendation</td>
</tr>
<tr>
<td>Neonatal Iron to prevent iron deficiency and iron deficiency anemia</td>
<td>High quality Evidence&lt;sup&gt;153-160&lt;/sup&gt;</td>
<td>Strong recommendation</td>
</tr>
<tr>
<td>Interventions</td>
<td>To Who</td>
<td>When</td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>2-5 years Pregnancy spacing- achieve optimal range</td>
<td>Women in Reproductive Age</td>
<td>All Preconception / interconception</td>
</tr>
<tr>
<td>Assessment of nutritional status using BMI</td>
<td>Women at risk to become pregnant</td>
<td>Preconception medical consult</td>
</tr>
<tr>
<td>Folic acid (FA) for the prevention of NTD’s</td>
<td>Women at risk or plan to become pregnant</td>
<td>3 months before conception</td>
</tr>
<tr>
<td>Multivitamins (MV) to prevent Congenital Malformation - non NTD’s-</td>
<td>women at risk or plan to become pregnant</td>
<td>3 months before conception</td>
</tr>
<tr>
<td>Prevention of Iron Deficiency Anemia (IDA)</td>
<td>All menstruating women: Adolescents and adults</td>
<td>Preconception / interconception (starting in postpartum) in area with high IDA prevalence</td>
</tr>
<tr>
<td>Treat Iron Deficiency Anemia (IDA)</td>
<td>All women in reproductive age</td>
<td>Preconception consult</td>
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</tbody>
</table>
The objective is to continue with interventions for a safe pregnancy: early assessment of the pregnant woman and partner as early as possible [no later than first trimester] by a skilled HCW to identify and modify risk factors and pathologies and achieve a healthy pregnancy and healthy child.

<table>
<thead>
<tr>
<th>Interventions</th>
<th>To Who</th>
<th>When</th>
<th>How</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess weight gain during pregnancy using pre pregnancy or first trimester pregnancy BMI— Under nutrition, overweight, obesity -</td>
<td>All pregnant</td>
<td>All medical consult and control</td>
<td>The recommended weight gain during pregnancy, depends on the measured pre pregnancy or first trimester of pregnancy BMI. Recommended weight BMI gain in all pregnancy</td>
<td></td>
</tr>
<tr>
<td>Folic Acid (FA) plus Multivitamins (MV) to prevent NTD’s</td>
<td>All pregnant women</td>
<td>All pregnancy and throughout lactation</td>
<td>Take orally daily for 3 months Preconception throughout pregnancy and throughout lactation. <strong>Women without risk factors for NTD’s</strong>: 3 months pre up to 3 months post conception MV with FA 0.8 to 1 mg. From 3 months post-conception, throughout pregnancy and lactation MV and FA take 0.4 to 1 mg / day. <strong>Women with a high risk factor for NTD’s</strong>: 3 months pre up 3 months post conception MV and FA 5 mg. From 3 months post-conception throughout pregnancy and lactation MV with FA 0.4 to 1 mg / day</td>
<td></td>
</tr>
<tr>
<td>MV to prevent CM other than NTD’s</td>
<td>All pregnant women</td>
<td>All pregnancy and throughout lactation</td>
<td>Idem at previous</td>
<td></td>
</tr>
</tbody>
</table>

| Recommended weight gain BMI gain in all pregnancy |
|---|---|
| <18.5 | 28-40 pounds |
| 18.5-<25 | 25-35 pounds |
| 25.0-<30 | 15-25 pounds |
| ≥30 | 11-20 pounds |

<table>
<thead>
<tr>
<th>Folic Acid</th>
<th>Reduce NTD and MV others non NTD anomalies.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>MV</th>
<th>Reduce preeclampsia</th>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>To Who</th>
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<th>How</th>
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<tr>
<td>Folic Acid (FA) plus Multivitamins (MV) to prevent NTD’s</td>
<td>All pregnant women</td>
<td>All pregnancy and throughout lactation</td>
<td>Take orally daily for 3 months Preconception throughout pregnancy and throughout lactation. <strong>Women without risk factors for NTD’s</strong>: 3 months pre up to 3 months post conception MV with FA 0.8 to 1 mg. From 3 months post-conception, throughout pregnancy and lactation MV and FA take 0.4 to 1 mg / day. <strong>Women with a high risk factor for NTD’s</strong>: 3 months pre up 3 months post conception MV and FA 5 mg. From 3 months post-conception throughout pregnancy and lactation MV with FA 0.4 to 1 mg / day</td>
<td></td>
</tr>
<tr>
<td>MV to prevent CM other than NTD’s</td>
<td>All pregnant women</td>
<td>All pregnancy and throughout lactation</td>
<td>Idem at previous</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Folic Acid</th>
<th>Reduce NTD and MV others non NTD anomalies.</th>
</tr>
</thead>
</table>

<p>| MV | Reduce preeclampsia |</p>
<table>
<thead>
<tr>
<th>Interventions</th>
<th>To Who</th>
<th>When</th>
<th>How</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia prevention</td>
<td>All pregnant women</td>
<td>as early as possible</td>
<td>Ferrous sulfate Tab 60-65 mg elemental iron (EI) + Folic Acid (FA) 0.4 mg PO 1 Tab / daily until end of pregnancy.</td>
<td>Reduce anemia and maternal and perinatal mortality</td>
</tr>
</tbody>
</table>
| Anemia treatment                      | All pregnant                                   | as early as possible        | Administer iron as per severity of anemia for the treatment of IDA among pregnant women. (Table 12). Administer Ferrous sulfate Tab 60-65 mg elemental iron (EI) + FA 0.4 mg  
In Anemia  
Mild : 1 tab once /day/ 3 months  
Moderate: 1 tab / BID/ 3 months  
Severe: 1 tab TID / 3 months. -Refer to Hospital.- Albendazole.-Assess for transfusion  
Replacement of iron deposits: once the IDA mild, moderate or severe is corrected should be given one cycle of EI 65 mg + FA 0.4 mg 1 tab / day / 3 months. | Effective control of the IDA in pregnant women, improves: cognitive development, iron deposits, physical and working ability, boosts immunity. Reduce maternal and perinatal mortality. |
| Prevention of Pre-Eclampsia and gestational hypertension: Calcium | All pregnant with low calcium intake (< than 4 cups of milk or dairy products daily). | from 12 weeks (useful in < 20 weeks) of gestation until birth | 1.5-2 g / day of elemental calcium, divided into 3 doses at the end of meals                                                                                                                           | Prevention of hypertension, pre-eclampsia, maternal and neonatal morbidity and mortality, especially those with high risk of pre-eclampsia. |
| Prevention of Pre Eclampsia and Gestational Hypertension: Aspirin during pregnancy |
| Pregnant with high risk of PE or hypertension: **ONE** of the following high risk factors is present: a. History of previous pregnancy hypertensive disorders, or previous PE. b. Chronic hypertension. c. Diabetes type 1-2. d. Chronic kidney disease e. Autoimmune disease: systemic lupus erythematosus, or thrombophilia or antiphospholipid syndrome. OR ≥ 2 of the following **MODERATE** risk factors: a. Primigravida b. Multiple pregnancy. c. Maternal age ≥ 40 years. d. Birth interval > 10 years. e. Mother or sister history of PE. f. BMI ≥ 35 kg/m² at first prenatal care. g. Urinary Tract Infection. h. Periodontal disease |
| Starting at 12 weeks GA (best ≤ 16 weeks, useful < 20 weeks GA) until birth. |
| Administer low-dose aspirin 75-100 mg PO at bedtime. |
| reduces the risk of: Preecclampsia, gestational hypertension, preterm birth, SGA and perinatal mortality |

| Prevention of Preterm Birth – Progesterone- | In pregnant women, with singleton pregnancy, with history of previous spontaneous preterm birth |
| starting at 16 weeks to 37 weeks of pregnancy |
| 17-Alfa hydroxyprogesterone caproate 250 mg IM once per week (the most used), or vaginal progesterone 100-400 mg / day or oral progesterone 100-200 mg / day PO. |
| IM progesterone reduce the risk for: perinatal and neonatal mortality, intraventricular hemorrhage. IM, vaginal and Oral progesterone reduces preterm NB < 37 weeks, preterm NB < 34 weeks, LBW, assisted ventilation, NEC, admission to NICU and prolonged pregnancy in average 4.5 weeks. |

<p>| Erythromycin in Preterm PROM |
| Pregnant with history of preterm birth, with PROM and not in labor, and without chorioamnionitis, pre- |
| In PROM &lt; 37 weeks GA and not in labor. |
| begin treatment before referral to higher level of resolution: 1. Erythromycin 250 mg every 6 hours for 10 |
| Reduce: chorioamnionitis, birth in 48 hours and 7 days, use of surfactant, oxygen and neonatal |</p>
<table>
<thead>
<tr>
<th>Indications</th>
<th>Treatment</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eclampsia, fetal distress or other contraindications to continue with the pregnancy</td>
<td>days or until delivery PO, whichever comes first. 2. Apply antenatal steroid as indicated (see antenatal steroid)</td>
<td>sepsis, RDS, intraventricular hemorrhage, NEC, and in developing countries can reduce neonatal mortality.</td>
</tr>
<tr>
<td>In preterm labor &lt; 37 weeks GA, without contraindication for use of uterine inhibitors (pre-Eclampsia, chorioamnionitis, fetal distress or fetal death, restriction of fetal growth or lethal CM):</td>
<td></td>
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<tr>
<td>In preterm labor &lt; 37 weeks GA</td>
<td>Initial dose: Nifedipine 10 mg PO if uterine contraction continues, 10 mg every 20 minutes, 2-3 times for a total of 40 mg. Maintenance dose: Nifedipine 10-20 mg PO, every 4-6 hours, based on contractions pattern, for 2-3 days. If the blood pressure is below 110 / 70 mm Hg, do not administer Nifedipine.</td>
<td>Reduce: birth less than 48 hours, preterm, maternal adverse effects, RDS, NEC, intraventricular hemorrhage, neonatal jaundice, and admissions to NICU.</td>
</tr>
<tr>
<td>Antenatal Corticosteroids for fetal pulmonary maturation</td>
<td>Indications for Antenatal Steroids. Threat of preterm delivery or preterm labor, premature rupture of membranes without chorioamnionitis, ante partum hemorrhage, hypertensive syndromes, any cause that justifies pre term delivery (fetal distress, diabetes, isoimmunization), pregnancy with elective caesarean section before 39 weeks GA.</td>
<td></td>
</tr>
<tr>
<td>between 26 to less than 36 weeks GA and in elective Caesarean section before 39 weeks GA.</td>
<td>Treatment</td>
<td>Reduces: neonatal mortality, cerebroventricular hemorrhage, necrotizing enterocolitis, admissions to NICU, early neonatal sepsis and delay in children's development and cerebral palsy.</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone 6 mg IM every 12 Hours total 4 doses or Betamethasone 12 mg IM every 24 hours total 2 doses. Threat of delivery within 24 hours, administer Dexamethasone or Betamethasone 12 mg IM every 12 hours total 2 doses. Start treatment immediately after diagnosis [can be used in women with diabetes and hypertensive disorders] unless there is imminent delivery [within one hour]. The objective is to attain one course of total dose of 24 mg before 24-48 hours before delivery. The administration of steroids up to one hour before delivery is also useful. The optimum effect is obtained between 48 hours to 7 days after administration of the total dosage of 24 mg. Rescue Course: 24 mg of steroids (2 courses maximum), same treatment if the previous course was administered 1-2 weeks earlier, the criteria to be indicated is met and if the delivery will occur in the following week.</td>
<td></td>
</tr>
<tr>
<td>Periodontal disease</td>
<td>All pregnant</td>
<td>Visit to Dentist two times during pregnancy first and third trimester</td>
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</tr>
<tr>
<td>Urinary Tract Infections</td>
<td>All pregnant</td>
<td>Best diagnostic for asymptomatic or symptomatic UTI is urine culture at 12-16 weeks GA, or first prenatal care. Other diagnostic method is the use of urine with positive nitrates and leukocytes esterase in every trimester.</td>
</tr>
<tr>
<td>STI's - Syphilis</td>
<td>Screen all pregnant women [serology] for syphilis</td>
<td>First prenatal visit, if it is negative repeat in the third trimester. A third screening is done upon admission before childbirth or in the postnatal period prior to discharge [in case of imminent delivery or fully dilated upon admission]. If the test for syphilis is positive mother and her partner should receive the treatment.</td>
</tr>
<tr>
<td>Labor Induction &gt; 41 weeks GA</td>
<td>in women with ≥ 41 weeks GA with no contra indication for labor induction [e.g. multiple pregnancy or polyhydramnios]</td>
<td>Induction labor with oxytocin (mainly used) or prostaglandins</td>
</tr>
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</table>
Life Course: Postnatal. The objective is maintain the continuity in the attention during delivery and neonatal period to identify and modify risk factors or pathologies for to get a newborn and child healthy.

<table>
<thead>
<tr>
<th>Interventions</th>
<th>To Who</th>
<th>When</th>
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<th>Why</th>
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</table>
| Prevention of Birth Asphyxia and consequences | All preconception and pregnant women | - Primary Prevention: before and during labor and delivery.  
- Secondary prevention of morbidity, mortality and long term sequelae: at birth  
- Tertiary prevention: newborn | Primary Prevention:  
- Preventing and promptly treating risk factors and fetal and neonatal morbidities (Table 22).  
- Improving access and quality of obstetric care (emergency included), mainly in the high risk pregnancy.  
Secondary prevention: Immediate resuscitation measures by trained personnel in cases of birth asphyxia.  
Tertiary prevention: improving early detection and treatment for children with disabilities, early stimulation and support for families | reduce neonatal mortality due to asphyxia and the hypoxic ischemic encephalopathy and neurological sequelae |
| Cardiopulmonary reanimation (CPR)  | NB with Birth Asphyxia          | Immediate at birth                        | Neonatal Cardio-pulmonary Resuscitation STEPS  
A. (Air) permeable airway, initial stabilization steps (heat source, head positioning, clear airways, drying and stimulation)  
B. (Breathing), initiates breathing.  
Ventilation with ambu and air.  
C. (Circulation), thoracic compression (cardiac massage)  
D. (Drug) Medications or volume Expansion. | Neonatal resuscitation in facility and Basic neonatal resuscitation in community reduce: early and neonatal mortality |
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<th>Why</th>
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<tbody>
<tr>
<td>Cord clamping until pulsation ceased</td>
<td>All neonates born by vaginal or cesarean section</td>
<td>between 1-3 minutes after birth or when pulsation ceased</td>
<td><em>Delayed clamping of the umbilical cord</em> is recommended in all births, while simultaneously start newborn essential care. In NB born by caesarean section, dry the NB, clothe and place on maternal thighs (or at a level slightly lower than the placenta), while waiting for pulsation to cease. If there is a need for early cord clamping to attend the NB, &quot;milk&quot; the umbilical cord 5 times, from placenta end towards the NB, for placenta transfusion, with similar results to delayed cord clamping</td>
<td>Increased birth weight, Hb concentration at 48 hours, iron deposit up 6 months. In preterm NB (24-36 weeks GA) reduces: need for transfusions due to anemia, intraventricular hemorrhage (all grades) and NEC</td>
</tr>
<tr>
<td>BF within the first hour of life</td>
<td>healthy NB, vaginal delivery or caesarean section</td>
<td>Within 1 hour of life</td>
<td>The healthy NB, vaginal delivery or caesarean section, must be placed immediately after birth near the mother breasts in skin to skin contact, until the first feeding is completed. The NB can be dried; Apgar evaluated and initiate physical examination, together with his mother</td>
<td>Reduced Neonatal mortality and increase breastfeeding.</td>
</tr>
<tr>
<td>Kangaroo mother Method (KMM)</td>
<td>To NB with LBW or preterm</td>
<td>The NB needs to be in stable condition: breathing spontaneously, without additional oxygen. The ability to feed (suck and swallow) does not constitute a fundamental requirement; you can start with feeding tube. As soon as the infant begins its recovery, discuss the desirability of KMM with the mother.</td>
<td>KMM is the care for premature NB or LBW through skin to skin contact with the mother. It’s an efficacious method and easy to apply promoting the health and wellbeing of term and preterm NB</td>
<td>Reduce: mortality risk, nosocomial sepsis, hypothermia, hospital stay, and improves physical growth and development.</td>
</tr>
<tr>
<td>Interventions</td>
<td>To Who</td>
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<tr>
<td>Neonatal Hypothermia prevention</td>
<td>All newborn</td>
<td>At birth</td>
<td>To implement the thermal protection of the NB in the hospital or at home, from birth and the first few days of life, apply the 10 steps recommended by WHO, the &quot;hot chain&quot; steps: 1. <strong>Warm delivery room.</strong> Maintain delivery room clean and warm (temperature between 25-28o C). 2. <strong>Dry the NB immediately at birth.</strong> With dry, warm, towels while the NB is on a warm surfacing. Maternal abdomen or thorax (skin to skin contact). 3. <strong>Skin to skin contact.</strong> Effective method to prevent loss of heat in term or preterm NB. After drying the NB placed on the mother's abdomen or thorax, who should be clean and dry, skin to skin contact, then cover with the same dry sheet used by the mother. 4. <strong>Early breastfeeding.</strong> Start BF within 1hour of life, on demand or every 2-3 hours while the BF is established. Breast milk is essential to provide: heat, nutrients and antibodies. Also skin to skin contact transfers heat to the NB. 5. <strong>Postpone the bath</strong> and weight. Bathing after 24 hour of life. Bathing immediately after birth causes hypothermia and is not necessary. 6. <strong>Clothe the NB and dress the bed appropriately</strong> depending on the room temperature. 7. <strong>Keep the mother and newborn together.</strong> Children born in hospital or at home, must remain with the mother 24 hours a day (accommodation - together), preferable in the same bed, in a room with temperature not less than 25° C. Rooming-in promotes breastfeeding, avoid hypothermia and hospital-acquired infections. 8. <strong>Maintain the hot temperature during transport</strong> keep the NB within normal temperature.</td>
<td>Reduce Hypothermia and neonatal complication and mortality risk</td>
</tr>
<tr>
<td>Cure of umbilical stump with Chlorhexidine</td>
<td>All born at home or hospital with high neonatal mortality (≥30 x1000 LB)</td>
<td>At first day for 7 days on NB born at home or hospitals</td>
<td>Applying Chlorhexidine 4% aqueous solution or gel on the umbilical cord, where there is high neonatal mortality (≥ 30 x 1000 LB) and in countries with limited resources</td>
<td>Reduce omphalitis and sepsis</td>
</tr>
<tr>
<td>Interventions</td>
<td>To Who</td>
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</table>
| Congenital syphilis elimination       | Screen all pregnant women [serology] for syphilis                      | First prenatal visit, if it is negative repeat in the third trimester. A third screening is done upon admission before childbirth or in the postnatal period prior to discharge [in case of imminent delivery or fully dilated upon admission]. If the test for syphilis is positive mother and her partner should receive the treatment. | Clinical Evidence of congenital Syphilis  
a. Asymptomatic born to mother with syphilis and did not receive appropriate treatment.  
b. Asymptomatic born to mother with syphilis with adequate treatment with titers 4 times higher than maternal titers.  
c. Asymptomatic born to mother with syphilis treated adequately, with no titers to measure against maternal titers.  
d. Asymptomatic born to mother with syphilis and: non-documented treatment, no reduction of titers, no syphilis testing [RPR] or positive re-infection | The early detection and treatment of maternal syphilis can significantly reduce: congenital syphilis, fetal death, preterm births and neonatal mortality, perinatal morbidity and mortality.  
The treatment of newborn reduce complications and mortality |
<p>| Vitamin D in breastfed neonates for the prevention of Vitamin D deficiency | term NB, preterm or NB with birth weight &lt; 2500 g with exclusive or partial BF | beginning between 3-5 days of life until the first year of life, when the child receives that amount of Vit D in foods | All term NB, preterm or LBW (birth weight &lt; 2500 g) with exclusive or partial Breastfeeding should be given 400 IU / day, Vitamin D orally. | to prevent Vitamin D deficiency and rickets in children and adolescents |</p>
<table>
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<th>How</th>
<th>Why</th>
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<tbody>
<tr>
<td>Vitamin A during neonatal period</td>
<td>Term or pre term NB, LBW in communities where children &lt;5 y, pregnant or lactating mothers suffer from: malnutrition, anemia, frequent infections, poor nutrition, eye problems [xerophthalmia, night blindness &gt; 1%] or where Vit A deficiency is greater than 20% among pregnant.</td>
<td>First 48-72 hours of life</td>
<td>Provide Vitamin A 50,000 IU PO to term or preterm, LBW NB in the first 48-72 hours of life. Dosage in NB with BW ≤ 1500 g or ≤ 32 weeks GA, Vitamin A 5000 IU, IM 3 times / week x 4 weeks</td>
<td>Reduced infant mortality due to all causes at 6th month of age and diarrhea mortality rate.</td>
</tr>
<tr>
<td>Neonatal Iron to prevent iron deficiency and iron deficiency anemia</td>
<td>Breastfed Preterm (&lt; 37 weeks GA), or LBW (&lt; 2500 g) newborns</td>
<td>Preterm (&lt; 37 weeks GA), or LBW (&lt; 2500 g) starting at one month up to 12 months of age. Newborn with birth weight &lt;1500 g, starting at 14 days - 1 month, up to 12-15 months of age Term NB EBF or partially breastfed starting at the 4th month of age</td>
<td>Preterm(&lt; 37 weeks GA), or LBW (&lt; 2500 g) should receive elemental iron supplementation at 2 mg/ kg/ day orally Newborn with birth weight &lt;1500 g: administer elemental iron at 2-4 mg/ kg/ day/ PO, to prevention deficiency. Term NB EBF or partially breastfed, should receive elemental iron at 1 mg/ kg/ day/ PO. Formula fed children do not need iron supplementation during the first 12 months of life. Use of whole milk formula is recommended after one year of age.</td>
<td>Children supplemented with iron have higher level of Hb, greater iron reserve and lower risk for developing iron deficiency and ID anemia, and behavioral problems.</td>
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</table>
### Acronyms, Abbreviations, Signs

<table>
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<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AGP</td>
<td>Alpha-1-acid glycoprotein</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CM</td>
<td>Congenital Malformations</td>
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<tr>
<td>cms</td>
<td>Centimeters</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>EBI</td>
<td>Evidence Based Interventions</td>
</tr>
<tr>
<td>FA</td>
<td>Folic Acid</td>
</tr>
<tr>
<td>FAD</td>
<td>Folic Acid Deficiency</td>
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<tr>
<td>FAO</td>
<td>Food and Agriculture Organization of the United Nations</td>
</tr>
<tr>
<td>GA</td>
<td>Gestational Age</td>
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<tr>
<td>GRADE system</td>
<td>Grading of recommendations, Assessment, Development, and Evaluation</td>
</tr>
<tr>
<td>HCW</td>
<td>Health Care Workers</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
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<tr>
<td>ID</td>
<td>Iron Deficiency</td>
</tr>
<tr>
<td>IDA</td>
<td>Iron Deficiency Anemia</td>
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<tr>
<td>IOM</td>
<td>Institute of Medicine</td>
</tr>
<tr>
<td>IU</td>
<td>International Units</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>Kg</td>
<td>Kilograms</td>
</tr>
<tr>
<td>LAC</td>
<td>Latin America and the Caribbean</td>
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<tr>
<td>LB</td>
<td>Live Births</td>
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<tr>
<td>LBW</td>
<td>Low Birth Weight</td>
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<tr>
<td>LGA</td>
<td>Large for Gestational Age</td>
</tr>
<tr>
<td>m</td>
<td>Meter</td>
</tr>
<tr>
<td>m²</td>
<td>Square meter</td>
</tr>
<tr>
<td>MA</td>
<td>Meta-Analysis</td>
</tr>
<tr>
<td>mcg</td>
<td>Microgram</td>
</tr>
<tr>
<td>MDG’s</td>
<td>Millennium Development Goals</td>
</tr>
<tr>
<td>MV</td>
<td>Multivitamin</td>
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<tr>
<td>n</td>
<td>Number</td>
</tr>
<tr>
<td>NB</td>
<td>Newborn</td>
</tr>
<tr>
<td>NGC</td>
<td>National Guidelines Clearinghouse</td>
</tr>
<tr>
<td>NICHD</td>
<td>National Institute of Child Health and Human Development</td>
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<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>NTD’s</td>
<td>Neural Tube Defects</td>
</tr>
<tr>
<td>OCM</td>
<td>Observable Congenital Malformation</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>PE</td>
<td>Preeclampsia</td>
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<tr>
<td>PNC</td>
<td>Prenatal Care</td>
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<tr>
<td>PO</td>
<td>Orally</td>
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<tr>
<td>RBC</td>
<td>Red Blood Cell</td>
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<tr>
<td>RCT</td>
<td>Randomized Controlled Trial</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>RDS</td>
<td>Respiratory Distress Syndrome</td>
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<tr>
<td>RR</td>
<td>Relative Risk</td>
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<tr>
<td>RRR</td>
<td>Relative Risk Reduction</td>
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<tr>
<td>SGA</td>
<td>Small for Gestational Age</td>
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<tr>
<td>SMO</td>
<td>Severe Maternal Outcome</td>
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<tr>
<td>SR</td>
<td>Systematic Review</td>
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<tr>
<td>USMR</td>
<td>Under Five Mortality</td>
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<tr>
<td>US/USA</td>
<td>United States / United States of America</td>
</tr>
<tr>
<td>PPV</td>
<td>Positive Pressure Ventilation</td>
</tr>
<tr>
<td>WC</td>
<td>Waist Circumference</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WRA</td>
<td>Woman/Women in Reproductive Age</td>
</tr>
<tr>
<td>&gt;</td>
<td>Greater than</td>
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<tr>
<td>&lt;</td>
<td>Less than</td>
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<tr>
<td>≥</td>
<td>Greater or equal to</td>
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<td>≤</td>
<td>Less or equal to</td>
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<tr>
<td>µg / dL</td>
<td>Nanogram / deciliter</td>
</tr>
<tr>
<td>p</td>
<td>P value</td>
</tr>
<tr>
<td>nmol/L</td>
<td>Nanomol/Litter</td>
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