Implementing calcium supplementation projects based on lessons learned

Calcium supplementation in pregnancy for prevention of pre-eclampsia

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1. What are preeclampsia, eclampsia and hypertensive disorders of pregnancy?

Hypertensive disorders of pregnancy (also called pregnancy-related hypertension) are defined as presence of elevated blood pressure with systolic pressure>140mmHg and/or diastolic pressure>90mm Hg during pregnancy. Pregnancy-related hypertension is a spectrum of conditions including chronic hypertension, gestational hypertension, preeclampsia, and eclampsia with varying management approaches rather than a specific diagnosis.

Specific diagnosis of the conditions across this spectrum depends on the onset of hypertension in relation to pregnancy as well as the presence of protein in urine (proteinuria). When onset of blood pressure elevation precedes the 20th week of pregnancy, a diagnosis of ‘chronic hypertension in pregnancy’ is made. Blood pressure elevation occurring after the 20th week of pregnancy in a woman previously known to have normal blood pressure is termed ‘gestational hypertension’. When significant protein is found in the urine (greater than 3g/24hr or dipstick>2) in addition to gestational hypertension, ‘preeclampsia’ is said to occur. The occurrence of convulsions or coma in a woman with preeclampsia is known as eclampsia (after ruling out other common causes of convulsion and/or coma).

Preeclampsia and eclampsia are the most dangerous hypertensive disorders of pregnancy. The underlying cause and biological processes leading to the symptoms of preeclampsia and eclampsia are not well understood. It probably is caused by multiple factors in both the mother and the fetus. Women are at higher risk of these conditions if the mother is very young (teenager), is having a first pregnancy after 35 years of age, is obese, is carrying twins, has Diabetes or has history of pre-eclampsia in herself or in her family. The only known cure for these conditions is delivery of the placenta. This usually raises a dilemma in management of these conditions because preterm birth is the number one reason that babies die in the first month of life.

2. How important are hypertensive disorders of pregnancy as a public health problem?

Hypertensive disorders of pregnancy are the 2nd leading cause of maternal mortality (pregnancy-related deaths) globally, and in addition, causes suffering to women and their families. Pre-eclampsia and eclampsia complicate about 2-8% of all pregnancies globally. About one out of every four maternal deaths in Latin America and the Caribbean, and about one out of every 10 maternal deaths in Africa and Asia have been attributed to pre-eclampsia and eclampsia.

3. How effective is calcium supplementation in preventing hypertensive disorders of pregnancy, including pre-eclampsia?

Recent systematic reviews and meta-analyses have reported that pregnant women taking at least 1 gram of supplemental calcium daily reduced their risk of developing hypertensive disorders by approximately half, with the effect varying largely by habitual calcium consumption and underlying risk of preeclampsia. The largest protective effects were found in populations with habitual calcium consumption less than 900 mg and clinical categories considered as having high risk of pre-eclampsia.

4. For whom is calcium supplementation recommended during pregnancy?

The World Health Organization recommends routine daily supplementation of 1.5 - 2 grams of elemental calcium for all pregnant women in populations with low calcium intake, particularly women at high risk of preeclampsia. Risk factors for preeclampsia include teenage pregnancy, elderly primigravida (first pregnancy after 35 years of age), maternal obesity, multiple gestation (e.g. twins), diabetes and family/prior obstetric history of pre-eclampsia.

5. The WHO recommends calcium supplementation in pregnancy in populations with low habitual calcium consumption. How do I know if calcium intake is low in my population of interest?

Low habitual calcium intake is defined as average habitual calcium intakes less than 900 mg of calcium per day. To illustrate this amount in terms of foods, 900 mg calcium could be provided by 3 cups (750 mL) of milk, or three servings of hard cheese such as cheddar, or 9 cups (more than 2 L) of cooked greens such as kale.

Routine administration to all pregnant women is advised when mean daily consumption is less than 900mg Ca/day in a population. Habitual calcium intake is poorly characterized in many developing countries. In settings where it has been studied, it has usually been found to be less than 900 mg except in few notable cases. Even high-income countries may not have habitual calcium intakes of 900 mg of calcium daily. It is reasonable to assume that the average population consumption is less than 900mg daily unless local studies are available and indicate otherwise.

6. At what gestational age should calcium supplementation be started?

The World Health Organization recommends starting supplementation at 20 weeks of gestation, because the research studies that have shown benefits started supplements in
mid-pregnancy. Based on what we know about the processes involved in preeclampsia, there might be extra benefit in starting supplementation earlier in pregnancy. There are on-going research studies investigating the feasibility and impact of initiating supplementation in the first few weeks of pregnancy.

**For how long should calcium supplements be taken by pregnant women?**

There are currently no limits on the duration of calcium supplementation. It is recommended that supplementation continue through delivery.

**What is the recommended daily dosage of calcium supplements for pregnant women?**

The World Health Organization recommends daily supplementation with 1.5 - 2 g of elemental calcium, based on the range of dosages administered in the clinical trials undertaken to date. At this point, scientists do not know the minimum effective dosage or optimal dosage for an individual patient.

**What time of the day is optimal for administration of calcium supplements in pregnancy?**

There are no current recommendations about the best time of day to take calcium supplements. However, calcium is absorbed better when supplements are taken in smaller (<500 mg) divided doses, for example in the morning and evening, rather than taking the whole dose all at once.

**Does calcium supplementation for pregnant women have any other benefit besides prevention of hypertensive disorders of pregnancy?**

Systematic reviews have reported that calcium supplementation may also improve bone mineral density in the infants of supplemented mothers, and reduce the risk of death for babies in the first month of life in developing countries.

**What are the side effects and risks associated with calcium supplementation in pregnancy?**

The latest systematic reviews of all the benefits and risks of calcium supplementation in pregnancy found a marginally elevated risk of a rare syndrome (HELLP, which stands for Hemolysis, Elevated Liver enzymes, Low Platelet Count) in calcium-supplemented women in two studies. The importance of this finding is not clear given the extremely low number of cases (less than 10 women out of over 12,000 participants) and the ways that different health care systems diagnose this condition.

Although there have been concerns about calcium supplements contributing to kidney stones, evidence from supplementation trials so far do not support an increased risk of kidney stones or other adverse side effects when calcium supplements are used as recommended.

**There are many kinds of calcium supplements available. How do I know which one is best?**

Calcium comes in several forms, and the best choice among the types of calcium supplements depends on consumer preferences, and the balance between concern for cost and ease of supplement delivery.

Calcium carbonate and calcium citrate malate have few side effects and are absorbed well. Several other types of calcium supplements are also available, but most of these are absorbed less well, or less is known about their side effects in pregnant women.

Calcium carbonate is cheaper and less bulky than calcium citrate malate (i.e. the pills can be made smaller) but its absorption might be less than that of calcium citrate malate if not taken around meal times.

**Are food-based strategies an effective alternative to calcium supplementation for prevention of hypertensive disorders of pregnancy?**

Calcium from food can also meet the needs of pregnant women. Calcium supplements are not a drug; rather they are useful to help meet the calcium demands of pregnancy in populations with habitually low calcium intakes. Consuming foods rich in calcium can also achieve this objective but in many areas of the world few calcium rich foods are commonly eaten every day. In many places, it may be difficult to rely solely on dietary changes to fill the dietary gap. Unlike other nutrients such as iron, excess calcium is not stored in the body in adults and increased absorption of calcium from the diet is the primary way that women meet the increased demands in pregnancy.

**Can calcium be combined with iron and folic acid?**

Some studies over short time periods (1-2 weeks) have found that when iron pills and calcium pills are taken together, less iron is absorbed. However, most long term studies of absorption did not show clinically significant negative effects on iron status. Taken together, these studies suggest that the body adapts to compensate for the inhibitory effects of calcium on iron absorption observed in the short-term. Therefore, taking iron-folic acid pills together with calcium supplements seems to be a reasonable way to reduce the complexity of taking more than one pill during pregnancy. Simpler protocols for taking calcium and iron pills together improve uptake and adherence by pregnant women.
Should pregnant women stop calcium supplementation when taking anti-malarial and other drugs?

Calcium is known to interact with a number of other drugs ranging from antibiotics to various classes of anti-hypertensive drugs. However, at this time there are no data or evidence to suggest that calcium interacts with typical anti-malarial drugs that are recommended for use during pregnancy. As in all instances, if other drugs are being used in pregnancy, a skilled care provider should be consulted about whether calcium supplements should be taken with other medications.

What is the likely cost of this intervention?

The cost of calcium supplements is generally higher than that of iron and folic acid but no systematic estimates of the cost of this intervention are currently available. The cost of implementing calcium supplementation as part of routine antenatal care would depend on many factors, including type of supplement used, effectiveness of existing healthcare delivery systems and local barriers to healthcare access.

Is the available information enough to guide program design and implementation? What further research is required?

Yes, currently available information and recommendations, such as this document, can be used to design functional programs and provide useful policy guidelines. However, because this is a new recommendation, further research will help to refine current recommendations and improve programs.

More specific research to further understand issues relating to nutrient-nutrient interactions, optimal dosage and optimal timing would be useful. Research on programmatic issues including cost and logistics of implementation, optimal delivery platforms, facilitation of adherence, and targeting mechanisms is ongoing and will inform programs.

The WHO has issued a strong recommendation for antenatal calcium supplementation to prevent preeclampsia and eclampsia based on current evidence that it can reduce maternal mortality and morbidity in developing countries. On-going research will help to refine the recommendation and its implementation, but evidence is sufficient to put policy and program plans in place now and make the most of this important opportunity to save lives.

Where can I find more information about calcium and the risks and prevention of hypertensive disorders of pregnancy?

More information is provided in the following references:


This project undertaken with support of the Government of Canada through the Department of Foreign Affairs, Trade and Development.
Guidance for prenatal calcium supplementation programming based on experiences with iron and folic acid supplementation

Are lessons learned from iron and folic acid supplementation (IFA) applicable to calcium supplementation?

Calcium supplementation, like IFA supplementation, involves daily micronutrient supplements for women to take during pregnancy and these will likely be distributed through prenatal or antenatal care (ANC). Pregnancy is thought to be a time when women can be motivated to take nutritional supplements to benefit the health of both mother and child and similar strategies might be used to promote both IFA and calcium supplements.Calcium supplementation programs are likely to face barriers similar to those of IFA programs with regard to supplies, coverage, and adherence. Because of these similarities, a great deal can be learned from past IFA experience and applied to future calcium supplementation initiatives.

There are also important differences. Calcium supplementation is intended to help prevent preeclampsia/eclampsia (PE/E), a dangerous condition but one that is uncommon relative to the anemia prevented by IFA. In addition, calcium supplements will not alleviate symptoms that are noticeable to the consumer, in contrast to IFA supplements which often remedy symptoms such as fatigue. As a result, promoting adherence to calcium supplementation may require different behavior change communication (BCC) approaches.

What policies are in place for preventive IFA and calcium supplementation during pregnancy?

Dietary intakes of iron and calcium are low for the majority of pregnant women in many countries. As a result, the WHO recommends a policy of supplementation for all women, rather than screening to target supplementation based on nutritional status.

**WHO Recommendations:**
- **IFA:** 30-60mg iron and 400ug folic acid daily during pregnancy and 3 months post-partum
- **Calcium:** 1.5-2 g of elemental calcium daily for all pregnant women in populations with usual calcium intakes averaging less than 900 mg per day.

Although not sufficient to guarantee success, governmental support of supplementation programs through development of national policy is an important and necessary step toward ensuring supplementation. Many countries have adopted either part or all of the WHO's recommendations for IFA supplementation. Iron supplementation is included in antenatal care policies universally but programs to improve folate nutrition have only been introduced in about 40 countries.
The WHO issued the recommendation on calcium supplementation in 2011 so there has been little opportunity to put in place national health policies on prenatal calcium supplementation for preventing PE/E. However, a number of countries are investigating the possibility of implementing such actions.

**How much progress has been made on ensuring that pregnant women receive adequate IFA supplementation?**

Progress has been made, but due to the varying measures used to evaluate IFA coverage and adherence, it is difficult to quantify. Large variation in IFA supplementation coverage is reported both within and among countries; national Demographic and Health Survey (DHS) data on the number of pregnant women who receive iron supplements range from 17% in Ethiopia to 93% in the Dominican Republic.

Despite significant gains in low income countries, the percent of pregnant women who receive and consume supplements at appropriate doses and timing remains unsatisfactory, partly because many women don’t start taking the pills until their second trimester. As a result, even women who report taking the pills are often not supplemented long enough to attain the full benefits of IFA supplementation. Lack of early and regular attendance at ANC and inadequate supplies of supplements remain important barriers to successful IFA supplementation. It is imperative that countries sustain positive momentum to increase coverage of IFA supplementation and facilitate progress in similar programs, such as calcium supplementation.

**What are the most important barriers to successful supplementation?**

The primary barriers to successful supplementation during pregnancy involve:

- Inadequate availability, quality and early and regular use of antenatal care (ANC)
- Poor supply of supplements due to ineffective procurement and distribution within the health care system

It is often assumed that poor adherence on the part of women is a major obstacle but while this can sometimes be a problem, experience has shown that the most important stumbling blocks occur even before women get their supplements. Barriers related to ANC and supplies of supplements are discussed in more detail below, followed by a discussion of barriers for adherence.

**Why is early and regular ANC attendance important for nutritional supplementation?**

Ensuring access to good quality ANC is an important component of Millennium Development Goal 5, “improve maternal health,” because it is a key entry point for pregnant women to receive multiple health promotion and preventive services including immunization, nutrition education and supplement distribution.

In the context of prenatal supplementation, early and regular ANC visits during which women are provided appropriate supplement doses and information are vital for ensuring adequate duration of supplementation and for promoting adherence to the prescribed regimen.

The WHO recommends an approach known as focused antenatal care (FANC), consisting of four ANC visits, starting in the first trimester, and emphasizing quality and individualized care.

Unfortunately, implementation of this strategy is far from universal and antenatal health services are severely underutilized. In low-income countries during 2005-2012, only 37% of pregnant women attended ANC four or more times, and trend data indicate little improvement in the past decade. The majority of women who do access services do so only in their late second or third trimesters, too late to fully benefit from many of the preventive interventions available or to identify early risk factors.

**What are the barriers to early and regular ANC attendance?**

Even among women who do attend ANC, few book as early or as often as recommended for FANC, limiting timely access to micronutrient supplementation. Societal norms mean that pregnancy is often not acknowledged until the second or third trimester, presenting cultural and psychological barriers to attending ANC earlier in pregnancy.

The reasons for underutilization of ANC are multi-factorial and include the following:

- A belief that ANC services are unnecessary or of poor quality
- Preference for consulting traditional birth attendants (TBAs) or family members
- Distance, lack of transportation or other geographic barriers (ANC use is often lower in rural areas)
- Financial constraints
- Concerns about long wait times
- Anxieties about communicating and interacting with health care providers
- Discomfort or religious restrictions related to examination by male providers
- Women’s lack of control over their own health care decisions
- Lack of support from the husband or family
- Hesitancy about acknowledging pregnancy in first trimester combined with the public nature of clinic attendance in many communities

**What are the successful strategies for improving utilization of ANC?**

Improving utilization depends in part on ensuring the availability of good quality ANC. Recommendations for increasing the quality of care include increased availability and quality of equipment and supplies, well-trained staff, evaluating and rewarding employee performance, improving communication at all levels and cultivating good patient-provider relationships.

Access to ANC can be enhanced by eliminating user fees, bringing basic ANC services to women in rural areas, expanding ANC services to help reduce waiting lines, providing child care services, offering services in multiple languages, and bringing basic services to the home and workplace.

Another strategy is to increase awareness of the importance of seeking timely ANC and find ways to increase comfort and willingness to disclose pregnancy earlier. In numerous countries, community health workers, traditional birth attendants, or trained midwives have been able to identify women early in their pregnancy and encourage them to seek ANC early and regularly, as discussed below (See FAQ 10).
Do women who attend ANC receive IFA supplementation?

Even if women attend ANC regularly during pregnancy, it does not guarantee that they will receive supplements or adequate information about their administration. For this to happen, the health system must ensure that (1) supplies of supplements are available in facilities, (2) staff provide adequate amounts of supplements to women during their ANC visit, and (3) staff provide effective counseling to help women remember to take supplements and to prepare them for possible side effects.

The multiple challenges that confront efforts to ensure adequate supplies of the appropriate micronutrient supplements at the facility level are discussed below (See FAQ 9 & 10). Once facility-level supply is ensured, provision of supplements and information during an ANC visit depends on staff training, supervision, and setting priorities. Health staff may not be adequately trained on the supplementation protocol or effective counseling techniques. Due to work load or motivational factors, health staff may not have or take the time necessary to counsel women properly. Without supportive supervision to address such hurdles, supplementation will not be fully implemented within ANC.

Therefore it is common for pregnant women seeking care to receive inadequate doses of supplements and improper or no information about them. Those women who visit prenatal health services are often familiar with iron supplements, but commonly do not know why they are prescribed, are not told about possible side effects, and receive conflicting information about dosage.10, 11 These challenges will also need to be addressed for successful promotion of calcium supplementation.

Why is the supply of supplements a barrier?

Ensuring adequate and reliable supplies depends on multiple people, organizations, and regulations and is therefore one of the major challenges facing efforts to increase coverage of supplementation programs. At the national level, responsibility for procurement of IFA may be unclear due to lack of coordination among government departments and in some cases, among international organizations who provide supplements on an interim basis.

Confusion about the most appropriate formulations and dosages for preventive supplementation can mean that the proper supplements are not included on a country’s list of essential drugs. Formulations must of course be clinically-effective, but there are other factors to consider. It is also important that the supplies procured are acceptable to women, thereby avoiding barriers related to supplement appearance, taste, shelf life and packaging.6, 10 Limited funding for supplements in national budgets is another hurdle for IFA and calcium supplementation and cost can influence which formulations are procured.

The supply problem is not limited to inadequate procurement at the national level, but also includes uneven distribution of tablets. Poor communication between facilities, imprecise targeting and lack of a demand-based supply system (see FAQ 10) lead to sporadic and inadequate supplementation coverage.

What are successful strategies for improving the supply of supplements?

A number of strategies are suggested for ensuring a continuous supply and effective delivery systems for supplements.10 An effective management system requires listing IFA (or other micronutrient) supplements as essential medicines and ensuring adequate buffer stocks. Many countries use a “push” or centralized supply-driven system for supplement distribution, meaning that supplies at the national level determine what will be distributed. However, it is recommended to also include a “pull” or demand-driven component in which distribution is based on regular monitoring of needs at the facility level.

This requires communicating local needs to regional or national levels so that supplies can be procured in advance. In addition, to maintain supplies at the local level, quality control must be in place in each facility, and tablets must be stored properly and monitored regularly to ensure timely restocking.

Nicaragua provides an example of how implementing these strategies to address the supply issues with IFA can increase supplement coverage and reduce anemia. Updated technical guidelines listing IFA supplements as essential medicines, efficient systems to procure and manage supplement stocks, and universal (no screening) distribution through several channels were successful in ensuring that women did not encounter difficulties in accessing iron supplements either at health posts or at local pharmacies.12 Similar systems will be needed to ensure adequate supplies of calcium supplements.

Are there other strategies for delivering micronutrient supplements to pregnant women outside of facility-based ANC?

There have been many successes in programs using alternative modes to reach women. Trained midwives, traditional birth attendants, and other community-based outreach workers can distribute IFA supplements,6, 8, 10 encourage women to attend ANC, and monitor their adherence with supplementation. For example, in the Philippines, Village Health Workers were trained to counsel women on iron pills and monitor compliance, partnering with professional health workers to distribute pills with great success.13 Nicaragua’s successful IFA supplementation program included distribution through multiple channels including ANC clinics, health posts, pharmacies, and community-based workers.4 Similar strategies were used in Thailand where pregnant women received IFA at ANC visits and village health volunteers helped to encourage compliance and visits to ANC.4 In Ethiopia’s Health Extension Program, local young women are trained to become Health Extension Workers who provide limited services within rural communities and successfully encourage model health behaviors including utilization of ANC services.14

What are the barriers to adherence, once women receive their supplements?

Cultural beliefs and norms can hinder adherence to supplementation. Women may avoid supplements because they believe the pills can cause miscarriages, large babies and difficult deliveries, or they associate iron with more bleeding at delivery. Cultural norms may underlie preferences for herbal tonics and other home remedies and avoidance of pills during pregnancy.4, 6, 8, 10 Motivation may be limited by lack of awareness of anemia (even among women who experience symptoms) and lack of explanation...
of the benefits of IFA. Symptoms of anemia may be seen as a natural part of pregnancy, lowering the demand for treatment. Similarly, symptoms of preeclampsia such as swelling of limbs are often seen as a normal part of pregnancy. Motivating women to take calcium supplements may be challenging if women and health workers do not view preeclampsia or eclampsia as risks or understand the role of supplements in preventing these conditions. In some countries, symptoms of eclampsia such as convulsions are believed to be due to evil spirits and thus unlikely to be seen as preventable with supplements.

Lack of adherence may result from forgetfulness, misunderstanding instructions, intentional overdosing, sharing the pills with family and friends or frustration about the frequency and number of pills prescribed. Once women start to feel better due to the effectiveness of IFA they may stop taking the supplements. Calcium supplementation differs in that women are unlikely to experience symptoms from which they will recover; however it is still possible that women may perceive changes in their health and decide that the supplements are no longer needed.

Physical and organoleptic qualities (taste, smell, etc.), the form of micronutrients, dosing, ease of use, packaging, and perceived health effects can affect adherence. Side effects can be a deterrent to adherence, particularly when one is not warned about them. Iron supplements may cause gastrointestinal side effects such as nausea, vomiting, constipation, diarrhea and abdominal distress. Calcium supplements can also cause mild gastrointestinal side-effects, such as constipation. However, the negative effect of side effects on adherence may be overestimated; with proper counseling women have been found to be willing to overcome any dissatisfaction with the side effects and continue to take IFA tablets. The same is expected to be true for calcium supplementation.

What strategies have been successful in improving adherence?

When women are given high quality supplements with correct information about health benefits and possible short-term side effects, and when they have the tangible experience of improved well-being from using the pills, they often are willing to continuously take the tablets.

Improving patient-provider relationships can aid in compliance to supplementation and it is important for health providers to use behavior change communication to give clear messages about the importance of taking the pills, directions for taking them, and warnings about possible side effects. Health care workers should be trained to use tested, culturally appropriate messages in all communication efforts.

Community-based health workers or volunteers can be valuable for bringing these messages to those who have limited access to health facilities. Including communities, community leaders, traditional healers, and families (especially husbands) in the discussion and promotion of the program can facilitate acceptance of supplements. Motivating information about the importance of supplements can also come from other sources. Radio and bus advertisements have been successful in Nigeria and promotion materials like flyers and posters have been shown effective in the Philippines. Memory aids and follow-up by health workers can also be helpful in reminding women to take the supplements regularly throughout pregnancy. For example, calendars used to mark daily intake of iron supplements have been successful for some women. It is essential that health staff, women, and other community members be consulted on their views and suggestions for the design of accessible programs and motivating health messages. Learning from successes in promoting IFA can be a starting point, but approaches will have to be adapted to calcium supplementation and to the contexts in which programs are implemented. Local input will be essential for this process.

REFERENCES


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