Essential fatty acids in maternal and infant nutrition

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Introduction

In many developing countries of the world and more especially in the countries of South Asia, the major nutritional problems that are now being encountered on a public-health scale are those related to mothers and infants. Maternal mortality rates in these countries range from 140 to 540; almost a third of infants are of low birth weight (<2.5 kg) and over 50% of under-fives are “stunted”\(^1\). The latest National Family Health Surveys data shows a maternal mortality rate of 540 in India. Thus, more than 100,000 women in India die each year due to pregnancy related causes.

Low birth weight is multifactorial in its causation. Factors such as low energy intake, low weight gain in pregnancy, low pregnancy weight, short maternal stature, anaemia, infections and smoking have all been identified as possible factors. The studies of Barker et al.\(^2\) have revealed disturbing long-term implications of intra-uterine growth retardation and low birth weight – namely predisposition to chronic degenerative diseases in adulthood. Retardation of growth and development at the intrauterine stage and in early infancy are perhaps the most urgent public health nutrition problems confronting many developing countries today.

Household diets of poor communities in these developing countries are deficient in a wide range of nutrients and stand in need of overall improvement. That good maternal nutrition status – at the preconceptional and post-conceptional stages, is important for maternal health, and foetal development, is now well recognised. However, precise information as to the crucial nutrients involved in ensuring optimal nutrition in pregnancy, lactation and in infant/child development could provide practical leads to public-health agencies as to the specific directions in which dietary improvement must be attempted. It is in this context that the emerging knowledge on the importance of essential fatty acids in maternal and infant nutrition is of great practical relevance.

In this presentation, we briefly review (i), the current knowledge regarding the role of essential fatty acids in maternal and infant nutrition; (ii), the current state of maternal and infant nutrition in poor communities; and (iii), address the question of how the emerging knowledge with respect to essential fatty acids could be usefully applied towards the improvement of maternal and infant nutrition.

Essential Fatty Acids

Polyunsaturated fatty acids (PUFA) include the parent essential fatty acids namely linoleic acid LA (n6) and \(\omega\)-linolenic acid ALNA (n3) and their long-chain more unsaturated derivatives. The parent essential fatty acids LA and ALNA cannot be synthesized in humans and therefore, need to be consumed as part of the diet. They are converted into their desaturated derivatives as indicated in Fig. 1. Both n3 and n6 fatty acids have common enzymes in their metabolic pathways; n3 fatty acids usually have higher affinity for the enzymes than the n6 fatty acids. The rate limiting enzymes in the desaturation process is the \(\Delta-6\) desaturase. This enzyme is under the control of many dietary and hormonal factors. The most important PUFA of the n6 series are dihomogammalinoleic acid (DHGLA) and arachidonic acid (AA) and these are the precursors of the eicosanoids of ‘1’ and ‘2’ series respectively. The important PUFA of the n3 series are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA (to which DHA can be reconverted) is the precursor of the eicosanoids of ‘3’ series.

Eicosanoids derived from these precursors are highly active compounds. The eicosanoids cascade consists of (a) cyclic products generated by cyclooxygenase – such as prostaglandins, prostacyclin and
acid efficiency is believed to contribute to poor placental function and arachidonic acid and DHA have been reported in the circulation of low birth weight new-borns and there is also evidence of vascular pathologies in the placenta of low birth weight babies. Essential fatty acid deficiency is believed to contribute to poor vascular growth and consequent rupture and coagulation in blood vessels leading to infarctions in the placenta that are believed to result in impaired placental functions and low birth weights. Arachidonic acid is essential for the structural integrity of the vascular endothelium. Arachidonic acid is the precursor for the synthesis of prostacyclin, which prevents thromboxane filtration. Through a proper balance between n3 and n6 fatty acids in the endothelium, vasoconstrictors and thrombogenic activities are influenced. Low birth weight and
prematurity are associated with a high incidence of neuro developmental disorders and disabilities. A positive correlation between arachidonic acid level in circulation and birth weight as also between duration of gestation and DHA level have been demonstrated. Reduced levels of arachidonic acid in maternal and cord blood phosphoglycerides are associated with low birth weight, low head circumference and low placental weight. High fish oil intakes have been shown to be associated with longer gestation and higher birth weight. Intervention studies with fish oils have also indicated that long-chain n3 fatty acids have an important role in ensuring normal birth weight. These observations point to the need for ensuring adequate nutritional status with respect to essential fatty acids in pregnancy. Indeed proper attention to adequate intake of essential fatty acids could be as important as attention to iron and folic acid. We will revert to this aspect later in this paper.

**Lactation**

Mature human breast milk is a good source of essential fatty acids of both the n6 and n3 series. A normal well-nourished woman putsforth adequate amounts of these acids needed for her infant in her breast milk as shown in data in Table 2. However, there is need for more information on the adequacy or otherwise of fatty acids in human milk of undernourished mothers. In a normal well nourished woman the fat-stores accumulated during pregnancy by themselves could provide a significant proportion of the essential fatty acids of milk at least during the first 3 months of lactation. Undernourished women may be expected to have accumulated relatively less fat-stores during pregnancy. Fat output in milk is variable and depends on maternal nutrition and prolactin secretion. It has been estimated that the mother's diet should provide 3 to 5 g of essential fatty acid daily to ensure adequate concentration of essential fatty acids in milk. In the absence of adequate intake of foods rich in essential fatty acids including fish, green leafy vegetables and pulses, essential fatty acids in breast milk of undernourished mothers could fall short of the requirements for normal infant growth and development. It is estimated that as many as six to ten thousand synaptic connections between neural cells are made in the post-natal period and early infancy. The basic materials required for this major operation are the essential fatty acids of human milk. The child's eventual state of mental development may well depend on the adequacy of supply of the needed fatty acids at this crucial stage of development.

**Neural development**

Almost two-thirds of the structural material of brain is lipid composed of cholesterol and phosphoglycerides rich in arachidonic acid and DHA. It is, therefore, understandable that dietary supply of EFA is limiting for brain growth. In the rods of the retina, DHA accounts for 50-60% of the phosphoglycerides embedding rhodopsin and the G-Protein. DHA is, therefore, central to receptor and neural transmission system on which brain function depends.

Studies on rhesus monkeys subjected to n3 fatty acids deficiency revealed that progressive depletion of docosahexaenoic acid from neural and retinal phospholipids followed by significant impairment of visual acuity, abnormalities in the electroretinogram and polydysxia.

Evidence indicates that both n3 and n6 fatty acids are limiting for brain growth and that neural integrity can be permanently disturbed by deficiency of both n6 and n3 essential fatty acids. Intrauterine growth retardation caused by n6 and n3 deficiency in pregnancy may thus affect both physical and mental development of the infant.

The above observation point to the important role of essential fatty acids in ensuring maternal nutrition, good pregnancy outcome and optimal growth and development of the offspring in the intrauterine phase and in the infancy.

**Low birth weight and intra-uterine retardation in poor communities**

Probably the highest incidence of low birth weight deliveries in the world occurs in poor communities in South Asia (including India, Pakistan, ...).
Bangladesh\textsuperscript{40,42,45,47}, Nepal\textsuperscript{40,48}, Sri Lanka\textsuperscript{40,42,45} \text{and} Maldive\textsuperscript{40}. There have been several reported studies on birth weights from these countries. The major conclusions that emerge from these studies are:

1) The gestational age of live born infants in poor communities appears to be significantly shortened as compared to those in the developed countries. Infants born prior to 37 weeks of gestation is just 5\% in developed countries (USA\textsuperscript{49} and Norway\textsuperscript{30}) as against 12-14\% births in India\textsuperscript{51}.

2) The incidence of low birth weight in full term deliveries in South Asian Countries is significantly much higher than the incidence reported from the developed countries. Thus, in a study involving over 20,000 full-term deliveries, the incidence of low birth weights was as high as 25\% as against 6-7\% in developed countries\textsuperscript{53}. The Nutrition Foundation of India carried out a study in 1998, which involved nearly 15,000 births that took place in a major hospital in Delhi catering to the poorest segments of the population\textsuperscript{55}. The result show that the high incidence of low birth weight deliveries even in full-term infants born after the 37 weeks of gestation in poor communities is to a considerable extent, a reflection of relative shortening of the gestational period. Nearly 34\% of all deliveries had taken place 37-38 weeks of gestation and 44\% after the 39\% week of gestation.

3) On the other hand, even in developing countries among the affluent sections of the population the incidence of low birth weight deliveries is apparently of the same order as observed in the developed countries. Thus a study\textsuperscript{54} by Nutrition Foundation of India showed that only 6\% of the infants among the affluent sections of Indian population were of low birth weight, indicating clearly that socio-economic factors, particularly undernutrition play the determining role.

As was pointed out earlier, low birth weight is probably of multifactorial origin. The outstanding common feature in poor communities associated with low birth weight is, however, maternal malnutrition\textsuperscript{55-56}.

**Essential fatty acids in Indian diets**

The important question from the point of view of present discussion is how adequate are the diets of poor pregnant women in India with respect to the essential fatty acids content. Pioneering studies on the essential fatty acids content of habitual Indian diets have been carried out by Ghafforunissa\textsuperscript{63} and Achaya\textsuperscript{64} and these studies provide a fair picture of the essential fatty acids intakes in Indian diets.

Diets of the poor Indian communities are largely cereal and pulse-based. Vegetable oil extracted from oil seed used as cooking fat is the major source of (visible) fat in the diet. The intake of such vegetable oils hardly exceeds 10 g per head per day. While in most poor households a single type of oil is used, in some others different types of vegetable oil may be employed depending on the food to be cooked. Apart from vegetable oils other sources of fat like meat and fish do not figure largely in the diets of poor households. Moreover, a considerable proportion of the Indian population is vegetarian. Milk intake is also marginal in poor households. All this may suggest that the intake of the essential fatty acid is highly inadequate in poor Indian diets.

However, careful analytical studies in recent years have shown that this is not the case. The picture with regard to overall essential fatty acids intake in poor Indian diets is however, reasonably bright in the light of recent studies. The major components of the Indian diet like cereals, pulses, tubers and vegetables are good source of invisible fat (meaning fat, which is an integral part of grain). Invisible fat was earlier not recognised because it was poorly analysed and detected for the reason that tightly bound structural lipid is not easily extractable by conventional methods. Achaya\textsuperscript{64} had computed that 10-15 en % (a level of fat that would provide as much as 10-15\% of the total energy value of the diet) is present in the invisible form. Invisible fat is a good source of LA and ALNA. For this reason Achaya considered poor Indian diets were reasonably adequate to meet essential fatty acids requirements in a normal subject. Using accurate method of extraction and gas-chromatography analysis Ghafforunissa\textsuperscript{63} found that the cereals contain 3\% and pulses 2\% of invisible fat and that on an average cereals provide 1.3\% LA and 0.5\% ALNA, pulses 1.2\% LA and 0.25\% ALNA. With an intake of around 500 g of cereals, diets could thus provide 7 en % of invisible fat 2.2\% of LA and 0.16 en % ALNA. Ghafforunissa\textsuperscript{65}, however, argues that while the present level of essential fatty acids even in poor Indian diets would thus meet normal requirements, they could be inadequate in pregnancy and lactation. She had computed that over and above the invisible fat present in the diet an intake of vegetable oil of the order of 30 g in pregnancy and 45 g in lactation would be necessary to fully meet requirements. On the basis of this computation it
could be concluded that poor Indian diets are deficient in essential fatty acids despite the substantial contribution of invisible fat from cereals, pulses, tubers and vegetables in the case of pregnant and nursing women.

Studies on effect of dietary supplementation to mothers on pregnancy outcome

Several studies on the effect of dietary supplementation on pregnancy performance and delivery outcome has been carried out in the developing countries. Some of the results have been briefly reviewed below.

Energy supplement

In most of the earlier studies on the effect of dietary supplementation to mothers during pregnancy on pregnancy outcome, the basic hypothesis had been that maternal energy intake could be a major determinant of intrauterine growth and foetal nutrition. Thus, Iyengar\(^{65}\) had shown that dietary supplements providing 500 additional calories per day even in the last 6-8 weeks of gestation to pregnant women habitually subsisting on low energy intake could bring about significant improvement in the birth weight of their offspring. Following this, several studies on the effect of dietary energy supplementation, had been carried out in India\(^{66}\), Sri Lanka\(^{67}\), Tha\(i\)wan\(^{68}\), Guatemala\(^{69}\), USA\(^{70}\), Mexico\(^{71}\), Canada\(^{72}\), Indonesia\(^{73}\) and Gambia\(^{74}\). The results of these studies have been confusing and contradictory. While some studies have reported increase in birth weight of offspring ranging from 40-320 g, following on energy supplementation, others have reported negative results. Kusin\(^{75}\) had shown that in malnourished mothers with very low energy intake, dietary energy supplementation during pregnancy contributed to increased weight gain in the mother but had no significant effect on the birth weight of the offspring. In situations of extreme under-nutrition, there could be a competition between maternal and foetal tissues for dietary energy supplements. Studies in Gambia\(^{74}\) had shown that heavy physical activity resulting in increased energy expenditure could have a significant impact on maternal and infant birth weight and supplements to such women with such marked caloric deficit resulted in greater weight gain to the mother with little impact on the birth weight of the offspring. The results of studies on the effect on dietary energy supplementation to the mothers on birth weight of their offspring have been equivocal and contradictory. That protein supplementation to maternal diets in pregnancy had no beneficial effect on the birth weight of offspring was shown by studies from USA\(^{70}\) and Guatemala\(^{69}\).

Most of these studies on macronutrient supplementation had not fully taken into consideration, the multiplicity of factors, which could affect the birth weights of infants such as maternal anaemia, infections and lack of physical rest in the last trimester of pregnancy.

Apart from these considerations in some of these earlier studies where dietary energy supplementation was attempted, the food sources of the so-called energy supplement could have actually provided apart from energy, quite a few micronutrients including essential fatty acids. If for example—the caloric supplement was largely based on cereals, the invisible fat in such cereals supplement could have provided essential fatty acids. It is possible that the absence of uniformity in the nature and the food source of supplement could account for the contradictory and equivocal results obtained.

Iron/Folic Acid/Zinc and Copper

The diets of poor pregnant women are deficient in a multiplicity of nutrients. In predominantly cereal based diets on which poor communities subsist the bioavailability of iron and zinc, for example, are low because of the high phytate content of cereals. Iron deficiency anaemia is, therefore, common in pregnant women of the poor communities of South Asia. Anemia is recognized to be a major factor associated with high maternal morbidity and mortality and routine administration of iron/folate in the last months of pregnancy is major public health approach in prevention of anaemia in pregnancy.

In this context it is important for us to determine to what extent iron/folate deficiency apart from anaemia, also accounts for intra-uterine growth retardation resulting in low birth weight. Leela Iyengar\(^{76}\) had shown that the birth weight of infants born to mothers receiving 200-300 micro gms of folic acid were significantly higher than those of mothers who did not receive such supplement thus showing a positive effect of folic acid supplementation on the birth weight of infants. Prema had shown that with iron supplementation, there was not only increase in haemoglobin levels of the mothers but also in the birth weight of the offspring\(^{66,77}\).

The relationship between maternal haemoglobin levels and birth weight of offsprings has also been
demonstrated in the form of a U curve with a progressive drop in the incidence of low birth weight deliveries with increase in haemoglobin levels from 8-11 g and an actual increase in low birth weight deliveries from that point with an increase of haemoglobin beyond 11 g. This latter increase may be due to hemoconcentration and consequently poor placental perfusion.

Striking changes in maternal serum zinc and maternal serum copper levels have been demonstrated in pregnancy. There is a slow but steady increase in the maternal copper levels and a corresponding slow fall in maternal serum zinc levels. Maternal-serum zinc levels reach lowest point at the time of delivery. It is only after six weeks of delivery that maternal serum zinc levels rise to the pre-pregnancy concentration. The rise in maternal serum copper levels is due to estrogen induced synthesis of ceruloplasmin and fall in zinc is due to altered binding affinity of zinc proteins. The fact that cord serum zinc levels are higher than maternal serum zinc levels is believed to indicate active transport of zinc across the placenta during pregnancy. However, the claims that in low birth weight infants cord plasma zinc levels are higher as compared to infants with normal birth weight has not been substantiated. There is no correlation between maternal copper and zinc levels and cord levels of copper and zinc.

It is thus clear that iron, folate acid, zinc and copper are micronutrients, which are actively involved in pregnancy.

The role of micronutrients and fatty acids — A final common pathway

The claims with regard to the positive effect of iron and folate supplementation on the birth weights and those regarding the effect of essential fatty acid supplementation need not necessarily be contradictory. There is evidence now that iron, folate acid, zinc and copper could all play a part in Δ6 and Δ9 desaturases system, and in the cyclooxygenases and lipoxygenases system that convert arachidonic acid to eicosanoids.

Studies on rats fed with fat free iron deficient diets on the one hand and studies on rats where iron deficiency was induced during pregnancy have indicated that conversion of 18:2 n-6 to their long chain derivatives may be blocked in iron deficiency and that the cyclooxygenases and lipoxygenases which convert arachidonic acid to eicosanoids are inhibited (Fig. 3). Thus, there is evidence in literature indicating an interrelationship between iron status and eicosanoid metabolism.

There is also similar evidence to suggest that zinc and copper may play a role in essential fatty acid and eicosanoid metabolism, zinc and copper being integral components of the Δ6 desaturase system (Fig. 3). Accumulation of 18:2 n-6 fatty acids in tissues of zinc deficient rats has been demonstrated. Copper has also been shown to play a part in the eicosanoid metabolism. It has been reported that folic acid administration increases the n-3 PUFA in plasma lipid fractions, in platelet, erythrocytes and intestinal phospholipids (Fig. 4).

It would seem reasonable to propose that the micronutrients like iron, copper, zinc and folic acid on the one hand and essential fatty acids on the other, do not act discordantly or independently of each other; but that, they are a part of a well coordinated symphony and not discordant solos.

These considerations underscore the fact that in undernourished population living on diets deficient in a multiplicity of nutrients including iron, folate, zinc, copper and essential fatty acids, it may be

![Diagram](image-url)
unwise to depend on either essential fatty acid supplementation alone or on iron and folate supplementation alone in improving the pregnancy outcome. Indeed, it had been shown in the context of low iron intake, essential fatty acid administration could aggravate anaemia. Our objective must be to ensure adequacy with respect to iron and folate on one side and essential fatty acids on the other. Green leafy vegetables like spinach fortunately are not only rich in iron and folate but also in essential fatty acids. Thus, the major approach towards combating of low birth weight among undernourished population may lie in the promotion of dietary diversification resulting in the increased intake of green leafy vegetables, pulses, milk and probably fish and not on isolated synthetic supplements.

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